AMERICAN BRACHYTHERAPY SOCIETY CERVICAL CANCER BRACHYTHERAPY TASK GROUP

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The American Brachytherapy Society (ABS) Gynecologic Cervical Cancer Task group has developed general criteria for the management of cervical cancer, designed to guide Radiation Oncologists and assist in making decisions regarding therapy. The complexity and severity of a patient's clinical condition should dictate the selection of appropriate treatment, but the availability of equipment and/or personnel may also influence the choice of therapy. Approaches classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria. The ultimate decision regarding the appropriateness of any treatment must be made by the attending physician. Highlights of the ABS recommendations are given below.

Gynecologic Brachytherapy:
The radiation dose delivered by brachytherapy is critical in curing patients of cervical cancer and has been the standard of treatment for over 100 years.

General Inclusion Criteria:
- Inoperable Stage IA1 and IA2 cervical cancer patients may be treated definitively with tandem-based brachytherapy alone.
- Inoperable Stage IB1 cervical cancer patients should be treated radically with brachytherapy in conjunction with external beam radiation. Concurrent chemotherapy may be considered at the physician's discretion and based on the presence of high risk features.
- Clinical stage IB2 - IVA Cervical Cancer should be treated radically with concurrent chemoradiation followed by brachytherapy.
- Stage IVB cervical cancer may be palliatively treated with brachytherapy with or without external beam to decrease the risk of severe hemorrhage or other life-threatening symptoms.
- Patients are treated with brachytherapy regardless of lymph node status, grade, presence of lymphovascular invasion, tumor size, age, or histology. Rarely, medical comorbidities may prohibit brachytherapy.
- The use of Intensity-Modulated Radiation Therapy (IMRT) or 3D conformal external beam radiation is not a substitute for brachytherapy.

Exclusion Criteria: *Absolute contraindications to radical treatment*
- Prior pelvic radiotherapy with brachytherapy
- Life expectancy < 6 months

Intraoperative Procedure:
- Standard brachytherapy procedure consists of dilating the cervical os, with ultrasound guidance to assist with tandem placement for difficult cases including cervix erosion, flattening, or cases where the os is not visible.
- Radiographic, CT, or MRI imaging to assist with dose prescription.

- Tandem and ovoid, tandem and ring or tandem and cylinders for intracavitary applications, inserted free hand
- Hollow interstitial needles inserted either freehand or with template or ultrasound guidance (e.g., template or guide holes in a ring applicator) for interstitial applications

Source Delivery System:

- HDR remote afterloader using iridium-192 in an outpatient setting
- PDR remote afterloader using iridium-192 in an inpatient setting
- LDR manually loaded or remote afterloader using cesium-137 and/or iridium-192 in an inpatient setting

Treatment Planning:

Dosimetry should be performed every time applicators are inserted to assess doses to the targets as well as the normal tissues, even if fixed geometry applicators are used. Failure to perform dosimetry can result in exceeding the normal tissue tolerance of the organs at risk.

- *Planning target volume:*
    - Point A should be reported for all cases regardless of the imaging modality utilized.
    - For institutions that utilize MRI, GTV for the cervix, high-risk CTV of the cervix plus tumor extension at the time of brachytherapy, intermediate-risk CTV of the cervix plus tumor extension at the time of diagnosis as defined by the GEC- ESTRO recommendations. Point A must always be reported, as should the D90, V100 and D2cc to the rectum, bladder and sigmoid.
    - For institutions that utilize CT, the width of the cervix and any parameterial extension should be contoured (HR-CTV-CT). The superior border of the cervix should extend at least 1cm above either the uterine vessels identified by IV contrast, or the location where the uterus begins to enlarge. If these cannot be identified, a height of 3cm should be contoured for the cervix.
    - Delineation of target volumes to be performed after insertion of tandem and vaginal applicators or interstitial applicator on images in the treatment planning computer.
    - Treatment planning for intracavitary applications should be performed after brachytherapy insertion and prior to treatment.
    - A pre-implant scan before the procedure may be performed for interstitial cases to assist with proper catheter placement.
    - Image-based volumetric information shall consist of CT, or MRI using contiguous slice acquisition with slice thicknesses $\leq$ 3 mm
    - Organs at risk to be contoured (including bladder, rectum, and sigmoid) are defined at the time of brachytherapy.
    - DVH information is used for assessment of coverage of the target and dose to organs at risk.
    - Reporting: Standard parameters reported in the GEC-ESTRO recommendations include the D2cc for the organs at risk; D90 and V100 for tumor.

- *Dosimetry*
    - Recommended prescription dosimetric parameters that should be met or exceeded.
    - Target coverage D90 should equal 100% of prescription
    - D2cc to the sigmoid <75Gy and D2cc to the rectum <75 Gy. No bladder parameter is currently defined. A D2cc <95 Gy has been reported.
    - *Dose homogeneity:*
        - The importance of dose homogeneity is unclear.
        - Efforts should be made to spare the bladder, rectum, and sigmoid.

Recommended Prescription:

- Low-dose-rate prescription may be in milligram-hours or in cGy to Point A or LDR primary treatment of 45-50 Gy external-beam plus 40-60 cGy/hr to a cumulative dose of 40-45 Gy.
- Goal TD should be >85 Gy. High-dose-rate typically prescribed in one of the following fractionation regimes: 5.5 Gy x 5, 6 Gy x 5, 7 Gy x 4
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Timing

- All treatment, including external-beam and brachytherapy, must be completed within 56 days from initiation of treatment.
- High-dose-rate brachytherapy commences after 39.6 Gy or 45Gy with up to 2 fractions being given per week during the conclusion of external beam and during the parametrial boost portion of treatment. Brachytherapy may be initiated earlier, but no earlier than approximately 20 Gy, if the physician determines that the applicator placed at this time point would provide adequate tumor coverage and sparing of normal tissues. Alternatively, if 45 Gy is delivered to the whole pelvis prior to brachytherapy, two brachytherapy insertions per week should be given to avoid treatment prolongation.
- Low-dose-rate implants commence after external beam treatment is completed with one implant per week.
- Chemotherapy is not typically given on the days of HDR brachytherapy but may be given with LDR brachytherapy

Post-Treatment Evaluation:

- Cervical cancer patients typically have Pap smear follow-ups every 3 months for 2 years, every 6 months for 3 years thereafter, then yearly.
- PET evaluation at 3 months has shown to be prognostic. The use of PET imaging at time points other than 3 months should be considered on an individual basis.
- Physical examination for recurrence or complications is necessary.
- Quality of life and patient satisfaction should be considered.
- Post-treatment biopsy may be needed to rule out recurrence.

SELECTED READING

I. PRACTICE PATTERNS

Erickson B, Eifel P, Moughan J, Rownd J, Iarocci T, Owen J. Patterns of brachytherapy practice for patients with carcinoma of the cervix (1996-1999): a patterns of care study. Int J Radiat Oncol Biol Phys 2005;63(4):1083-92.

Viswanathan AN, Erickson B. Three-Dimensional Imaging in Gynecologic Brachytherapy: A Survey of the American Brachytherapy Society. Int J Radiat Oncol Biol Phys (Epub July 2009)

HDR versus LDR

Stewart, AJ and **Viswanathan, AN**. Current Controversies in Brachytherapy for Cervical Cancer. Cancer 2006; 107(4):111-119.

II. TREATMENT PLANNING

A. Standard 2D

Tod, M.C. and Meredith, W.J. A dosage system for use in the treatment of cancer of the uterine cervix. Br. .I. Radiol. 1 I: 809-824, 1938

Wilkinson JM, Ramachandran TP. The ICRU recommendations for reporting intracavitary therapy in gynaecology and the Manchester method of treating cancer of the cervix uteri. Br J Radiol 1989;62(736):362-5.

B. 3-D Image Guided Brachytherapy

Textbook: Innovations in Image Guided Therapy for Gynecologic Radiation Therapy, Editors: AN Viswanathan, Erickson B, Pötter R, Kirisits C. Springer, 2010.

1. Contouring MR images with brachytherapy applicator in place:

Haie-Meder C, Pötter R, Van Limbergen E, Briot E, De Brabandere M, Dimopoulos J, Dumas I, Hellebust T, Kirisits C, Lang S, Muschitz S, Nevinson J, Nulens A, Petrow P, Wachter-Gerstner N. Recommendations from Gynaecological (Gyn) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. Radiother Oncol 2005; 74:235-245.

Pötter R, Haie-Meder C, Van Limbergen E, Barillot I, DeBrabandere M, Dimopoulos J, Dumas I, Erickson B, Lang S, Nulens A, Petrow P, Rownd J, Kirisits C. Recommendations form gynaecological (GYN) GEC ESTRO working group (II):

Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. Radiotherapy and Oncology 78:67-77, 2006.

2. Treatment Planning with MR images:

Kirisits C, Pötter R, Lang S, Dimopoulos J, Wachter-Gerstner N, Georg D. Dose and volume parameters for MRI-based treatment planning in intracavitary brachytherapy for cervical cancer. Int J Radiat Oncol Biol Phys 2005;62(3):901-11.

Chargari C, Magné N, Dumas I, Messai T, Vicenzi L, Gillion N, Morice P, Haie-Meder C. Physics contributions and clinical outcome with 3D-MRI-based pulsed-dose-rate intracavitary brachytherapy in cervical cancer patients. Int J Radiat Oncol Biol Phys. 2009 May 1;74(1):133-9. Epub 2008 Sep 5.

3. CT or US based treatment planning:

Viswanathan AN, Dimopoulos J, Kirisits C, Berger D, Pötter R., Computed tomography versus magnetic resonance imaging-based contouring in cervical cancer brachytherapy: results of a prospective trial and preliminary guidelines for standardized contours. Int J Radiat Oncol Biol Phys. 2007 Jun 1;68(2):491-8.

Erickson B, Albano K, Gillin M., CT-guided interstitial implantation of gynecologic malignancies., Int J Radiat Oncol Biol Phys. 1996 Oct 1;36(3):699-709.

S Van Dyk, D Bernshaw, Ultrasound-based conformal planning for Gynaecological Brachytherapy, Journal of Medical Imaging and Radiation Oncology. 2008; 52 (1) :77–84

Holloway CL, Racine ML, Cormack RA, O'Farrell DA, Viswanathan AN. Sigmoid Dose Using 3D Imaging in Cervical Cancer Brachytherapy. Radiotherapy and Oncology Epub Aug 6 2009

Lee L, Sadow C, Russell AH, Viswanathan AN. Correlation of Point B and Lymph Node Dose in High-Dose-Rate Cervical Cancer Brachytherapy. Int J Radiat Oncol Biol Phys, Epub Mar 13 2009.

Jones N, Rankin J, Gaffney D. Is simulation necessary for each high-dose-rate tandem and ovoid insertion in carcinoma of the cervix? Brachytherapy 3:120-124, 2004.

4. Clinical outcome with 3D based planning for cervical cancer

Pötter R, Dimopoulos J, Georg P, et al. Clinical impact of MRI assisted dose volume adaptation and dose escalation in brachytherapy of locally advanced cervix cancer. Radiother Oncol 2007;83(2):148-55.

Dimopoulos JC, Lang S, Kirisits C, Fidarova EF, Berger D, Georg P, Dörr W, Pötter R.

Dose-Volume Histogram Parameters and Local Tumor Control in Magnetic Resonance Image-Guided Cervical Cancer Brachytherapy. Int J Radiat Oncol Biol Phys 2009 Mar Epub.

Haie-Meder C, Chargari C, Rey A, Dumas I, Morice P, Magné N. DVH parameters and outcome for patients with early-stage cervical cancer treated with preoperative MRI-based low dose rate brachytherapy followed by surgery. Radiother Oncol. 2009 Jul 6 Epub.

II. Diagnostic Imaging

Hricak H, Gatsonis C, Coakley FV, Snyder B, Reinhold C, Schwartz LH, Woodward PJ, Pannu HK, Amendola M, Mitchell DG.Early invasive cervical cancer: CT and MR imaging in preoperative evaluation - ACRIN/GOG comparative study of diagnostic performance and interobserver variability.Radiology. 2007 Nov;245(2):491-8.

Mitchell DG, Snyder B, Coakley F, et al. Early invasive cervical cancer: tumor delineation by magnetic resonance imaging, computed tomography, and clinical examination, verified by pathologic results, in the ACRIN 6651/GOG 183 Intergroup Study. J Clin Oncol 2006;24(36):5687-94.

III. Applicator Selection

Erickson B, Jones R, Rownd J, Albano K, Gillen M. Is the Tandem and Ring Applicator a Suitable Alternative to the High Dose Rate Selectron Tandem and Ovoid Applicator. Journal of Brachytherapy International 2000;16:131-44.

IV. RADIOBIOLOGY

V. IMAGING QA

Katz A, Eifel PJ. Quantification of intracavitary brachytherapy parameters and correlation with outcome in patients with carcinoma of the cervix. International Journal of Radiation Oncology, Biology, Physics 2000;50(3):837-8.

VI. MORBIDITY

Eifel PJ, Jhingran A, Bodurka DC, Levenback C, Thames H. Correlation of smoking history and other patient characteristics with major complications of pelvic radiation therapy for cervical cancer. J Clin Oncol 2002;20(17):3651-7.

Georg P, Dimopoulos J, Kirisits C, Lang S, Berger D, Pötter R. The Predictive Value of Dose Volume Parameters in MRI Based Cervical Cancer Brachytherapy for Late

Adverse Side Effects in Rectum, Sigmoid and Bladder. Int J Radiat Oncol Biol Phys 2006;66(3):S42.

Georg P, Kirisits C, Goldner G, Dörr W, Hammer J, Potzi R, Berger D, Dimopoulos J, Georg D, Pötter R. Correlation of dose-volume parameters, endoscopic and clinical rectal side effects in cervix cancer patients treated with definitive radiotherapy including MRI-based brachytherapy. Radiother Oncol 2009; 91(2): 173-80.

Koom WS, Dohn DF, Kim JY, Kim JW, Shin KH, Yoon SM, Kim DY, Yoon M, Shin D, Park SY, Cho KH. Computed tomography-based high-dose-rate intracavitary brachytherapy for uterine cervical cancer: preliminary demonstration of correlation between dose-volume parameters and rectal mucosal changes observed by flexible sigmoidoscopy. Int J Radiat Oncol Biol Phys 2007; 68(5):1446-54.

Viswanathan AN, Racine ML, Cormack RA. Final results of a prospective study of MR-based interstitial gynecologic brachytherapy. Brachytherapy 2008;7(2):148.