National Imaging Associates, Inc.	
Clinical guideline **CERVICAL CANCER**	**Original Date: June 2013**
Radiation Oncology	**Last Revised Date: April 2019**
Guideline Number: NIA_CG_127	**Implementation Date: January 2020**

INDICATIONS FOR RADIATION THERAPY AND TREATMENT OPTIONS:

Definitive/Preoperative Radiation Therapy (NCCN, 2018)

- Stage IA –IA2– Brachytherapy (LDR or HDR) +/- 2D/3D-CRT (40-50 Gy; 28 fx max)
- Stage IB1 – Pelvic 2D/3D-CRT (40-50 Gy; 28 fx max) + brachytherapy boost
- Stage IB2-IIA – Pelvic radiation therapy 2D/3D-CRT (40-50 Gy; 28 fx max) + brachytherapy boost) and concomitant chemotherapy +/- adjuvant hysterectomy.
- Stage IIB-IVA – Pelvic and/or paraortic 2D/3D-CRT + brachytherapy + concurrent chemotherapy.
- Stage IVB – 2D/3D-CRT +/- brachytherapy for palliation only (symptom control)

Grossly involved unresected nodes may be evaluated for boosting with an additional 10-15Gy

Postoperative (Adjuvant) Radiation Therapy (NCCN, 2018)

- Patients found to have deep cervical stromal invasion, lymphovascular invasion and/or bulky primary tumors.
    - Pelvic 2D/3D-CRT (45-50.Gy; 28 fx max) +/-concurrent chemotherapy
- Patients with positive nodes, positive margins and/or parametrial invasion –
    - Pelvic 2D/3D-CRT (45-50. Gy; 28 fx max) + concurrent chemotherapy
    - Pelvic 2D/3D-CRT (45-50 Gy; 28 fx max) +/- vaginal brachytherapy boost (LDR or HDR) can be considered in women with a positive margin.

Local /Regional Recurrence (NCCN, 2018)

- No previous RT or outside previous RT fields
    - 2D/3D-CRT + chemotherapy +/- brachytherapy
- Previous RT
    - Intraoperative Radiation Therapy (IORT) for centralized disease
    - Possible Brachytherapy (LDR or HDR) for centralized disease < 2cm Tumor directed 2D/3D-CRT +/- chemotherapy if noncentral disease

Grossly involved unresected nodes may be evaluated for boosting with an additional 10-15Gy.

Unless otherwise indicated standard radiation fractionation consists of 1.8 Gy to 2.0 Gy per day.

TREATMENT OPTIONS REQUIRING ADDITIONAL CLINICAL REVIEW (NCCN, 2018):

Intensity modulated radiation therapy (IMRT)

IMRT is not indicated as a standard treatment option and should not be used routinely for the delivery of radiation therapy for cervical cancer. IMRT is strictly defined by the utilization of inverse planning

modulation techniques. IMRT may be appropriate for circumstances in which radiation therapy is indicated and

- Non-IMRT techniques cannot adequately deliver the radiation prescription without exceeding normal tissue radiation tolerance. The non-IMRT delivery is anticipated to contribute to potential late toxicity
- Tumor volume dose heterogeneity from non-IMRT techniques is such that unacceptable hot or cold spots are created

Requests for IMRT treatment delivery to the cervix will be reviewed for medical necessity prior to authorization based on the above criteria. Clinical rationale and documentation for performing IMRT rather than non-IMRT techniques must be provided for review. This includes a statement of medical necessity from the requesting provider and a dosimetric comparison plan addressing the approval criteria above.

The plan will:

- Demonstrate how non-IMRT treatment planning cannot produce a satisfactory treatment plan (as stated above) via the use of patient specific dose volume histograms and isodose plans.
- Provide tissue constraints for both the target and affected critical structures.

Stereotactic Body Radiation Therapy (SBRT)
Stereotactic Body Radiation Therapy is not a standard treatment option for the treatment of cervical cancer.

Proton Beam Radiation Therapy
Proton beam is not an approved treatment option for cervical cancer. Proton beam has not been proven superior treatment to conventional radiation therapy.

THE FOLLOWING APPLIES TO CMS (MEDICARE) MEMBERS ONLY:

For Proton Beam and Stereotactic Radiotherapy refer to Local Coverage Determination (LCD), if applicable.

BACKGROUND:
The role of radiation therapy in the treatment of cervical cancer has been long established through clinical trial, providing strong evidence of support as an effective cervical cancer treatment. The traditional approach utilizes external beam irradiation therapy to the pelvis ± periaortic lymph nodes, as well as some form of brachytherapy boost, based on clinical and pathologic factors. There have been improvements in radiation therapy technology, reducing dose to normal surrounding tissue (bladder, rectum, and small bowel), but the majority of the experience to date is based on a point A dosing system.

This guideline outlines several methods suitable for the employment of radiation therapy in conjunction with cervical cancer treatment. These include the use of three-dimensional conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT), image-guided radiation therapy (IGRT), and internal radiation (brachytherapy). Although intensity modulated radiation therapy (IMRT) is becoming

more widely available, the routine use in treating cervical cancer remains to be validated. IMRT may be useful when high doses are required to treat gross disease in regional lymph nodes. However IMRT should not be used as routine alternatives to brachytherapy for treatment of central disease in patients with an intact cervix. Although there have been significant advances in imaging, planning and treatment delivery, this must be tailored to a thorough understanding to the stage of disease, pathways for dissemination and recurrence risk. Most external beam treatments are delivered using a high-energy linear accelerator. Brachytherapy is generally delivered as either low dose permanent implant or high dose rate implant. Principles of radiation therapy for these guidelines closely follow what is recommended both by the American Brachytherapy Society (Cervical Cancer Brachytherapy Task Group), as well as in National Comprehensive Cancer Network Practice Guidelines for Cervical Cancer.

POLICY HISTORY:
Review Date: February 2019
Review Summary: Added and updated references

REFERENCES:

Albuquerque K, Giangreco D, Morrison C, et al. Radiation-related predictors of hematologic toxicity after concurrent chemoradiation for cervical cancer and implications for bone marrow-sparing pelvic IMRT. [Published online ahead of print May 12, 2010]. Int J Radiat Oncol Biol Phys. March 15, 2011; 79(4):1043-1047.

American Brachytherapy Society (ABS). Consensus Guidelines for Locally Advanced Carcinoma of the Cervix. Part I. General Principles. https://www.americanbrachytherapy.org/guidelines/Guidelines_Carcinoma_Cervix_Part1.pdf. Published 2012a. Accessed April 24, 2018.

American Brachytherapy Society (ABS). Consensus Guidelines for Locally Advanced Carcinoma of the Cervix. Part II. High-Dose-Rate Brachytherapy. https://www.americanbrachytherapy.org/guidelines/Guidelines_Carcinoma_Cervix_PartII.pdf. Published 2012b. Accessed April 24, 2018.

American Brachytherapy Society (ABS). Consensus Guidelines for Locally Advanced Carcinoma of the Cervix. Part III. Low-Dose-Rate and Pulsed-Dose-Rate Brachytherapy. https://www.americanbrachytherapy.org/guidelines/Guidelines_Carcinoma_Cervix_PartIII.pdf. Published 2012c. Accessed April 24, 2018.

American Cancer Society (ACS). What are the Key Statistics about Cervical Cancer? http://www.cancer.org/cancer/cervicalcancer/detailedguide/cervical-cancer-key-statistics. Published 2016. Accessed May 9, 2016.

American College of Radiology (ACR) Appropriateness Criteria®. Advanced Cervical Cancer. https://acsearch.acr.org/docs/70544/Narrative/. Reviewed 2012. Accessed June 3, 2015.

American College of Radiology (ACR) Appropriateness Criteria®. Early Stage Cervical Cancer. https://acsearch.acr.org/docs/70908/Narrative/. Date of Origin 2012. Accessed June 3, 2015.

American College of Radiology (ACR) Appropriateness Criteria®. Role of Adjuvant Therapy in the Management of Early Stage Cervical Cancer. https://acsearch.acr.org/docs/70543/Narrative/. Last Reviewed 2014. Accessed June 3, 2015.

Bentzen SM, Constine LS, Deasy JO, et al. Quantitative analyses of normal tissue effects in the clinic QUANTEC: An introduction to the scientific issues. Introductory paper. *Int J Radiat Oncol Biol Phys*. 2010; 76(3):S3-S9.

Chargari C, Magne N, Dumas I, et al. Physics contributions and clinical outcome with 3D-MRI-based pulsed-dose-rate intracavitary brachytherapy in cervical cancer patients. *Int J Radiat Oncol Biol Phys*. May 2009; 74(1):133-139. doi: 10.1016/j.ijrobp.2008.06.1912.

Chung YL, Jian JJ, Cheng SH, et al. Extended-field radiotherapy and high dose rate brachytherapy with concurrent and adjuvant cisplatin-based chemotherapy for locally advanced cervical cancer: A phase I/II study. *Genecol Oncol*. 2005; 97:126-135. http://dx.doi.org/10.1016/j.ygyno.2004.12.039.

Eifel PJ, Winter K, Morris M, et al. Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for high risk cervical cancer: An update of radiation therapy oncology group trial (RTOG) 90-01. *J Clin Oncol*. 2004; 22:872-880. doi: 10.1200/JCO.2004.07.197.

Haie-Meder C, Potter R, Van Limbergen E, et al. Recommendations from Gynaecological (Gyn) GED-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. doi:10.1016/j.radonc.2004.12.015.

Hasselle MD, Rose BS, Kochanski JD, et al. Clinical outcomes of intensity-modulated pelvic radiation therapy for carcinoma of the cervix. *Int J Radiat Oncol Biol Phys*. August 12, 2010; 80(5):1436-1445.

Holloway CL, Racine ML, Cormack RA, et al. Sigmoid dose using 3D imaging in cervical cancer brachytherapy. *Radiother Oncol*. 2009; 93(2):307-310. doi: 10.1016/j.radonc.2009.06.032.

Jackson A, Marks LB, Bentzen SM, et al. The lessons of QUANTEC: Recommendations for reporting and gathering data on dose-volume dependencies of treatment outcome. *Int J Radiat Oncol Biol Phys*. 2010; 76(3):S155-S160.

Jones ND, Rankin J, Gaffney D. Is simulation necessary for each high-dose-rate tandem and ovoid insertion in carcinoma of the cervix? Brachytherapy. 2004; 3(3):120-124. doi:10.1016/j.brachy.2004.07.001.

Kidd EA, Siegel BA, Dehdashti F, et al. Clinical outcomes of definitive intensity-modulated radiation therapy with fluorodeoxyglucose-positron emission tomography simulation in patients with locally advanced cervical cancer. [Published online ahead of print October 31, 2009]. Int J Radiat Oncol Biol Phys. July 15, 2010; 77(4):1085-1091.

King M, McConkey C, Latief TN, et al. Improved survival after concurrent weekly cisplatin and radiotherapy for cervical carcinoma with assessment of acute and late side effects. *Clin Oncol (R Coll Radiol).* 2006; 18:38-45. http://www.ncbi.nlm.nih.gov/pubmed/?term=King%2C+M.%2C+McConkey%2C+C.%2C+Latief%2C+T.N.%2C+et+al.+(2006).+Improved+survival+after+concurrent+weekly+cisplatin+and+radiotherapy+for+cervical+carcinoma+with+assessment+of+acute+and+late+side+effects.++Clin+Oncol+(R+Coll+Radiol).+18%2C+38-45.

Kirisits C, Potter R, Lang S, et al. Dose and volume parameters for MRI-based treatment planning intracavitary brachytherapy for cervical cancer. *Int J Radiat Oncol Biol Phys*. 2005; 62(3):901-911. doi:10.1016/j.ijrobp.2005.02.040.

Lee L, Sadow C, Russell AH, et al. Correlation of point B and lymph node dose in high-dose-rate cervical cancer brachytherapy. *Int J Radiat Oncol Biol Phys*. November 2008; 75(3):803-809. doi: 10.1016/j.ijrobp.2008.11.052.

Monk BJ, Tewari KS Koh WJ. Multimodality therapy for locally advanced cervical carcinoma: state of the art and future directions. *J Clin Oncol*. 2007; 25:2952-2965. doi: 10.1200/JCO.2007.10.8324.

National Comprehensive Cancer Network (NCCN). Cervical Cancer. 1.2018. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. October 2017. Accessed April 24, 2018.

Potter R, Dimopoulos J, George 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):148-155. doi:10.1016/j.radonc.2007.04.012.

Potter R, Haie-Meder C, Van Limbergen E, et al. Recommendations from Gynaecological (Gyn) GED-ESTRO Working Group (II): Concepts and terms in 3D image-based 3D treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. *Radiother Oncol*. 2006; 78:67-77. doi:10.1016/j.radonc.2005.11.014.

Rotman M, Sedlis A, Piedmonte MR, et al. A phase III randomized trial of post-operative pelvic irradiation in Stage 1B cervical carcinoma with poor prognostic features: Follow up of a gynecologic oncology group study. *Int J Radia Oncol Biol Phys*. 2006; 65:169-176. doi:10.1016/j.ijrobp.2005.10.019.

Shivnani AT, Rimel BJ, Schink J, et al. Cancer of the cervix: Current management and new approaches. *Oncology*. 2006; 15(12):1553-1560. http://www.ncbi.nlm.nih.gov/pubmed/?term=Shivnani%2C+A.T.%2C+Rimel%2C+B.J.%2C+Schink%2C+J.%2C+%26+Small%2C+W.+Jr.+(2006).+Cancer+of+the+Cervix+Current+Management+and+New+Approaches.+Oncology%2C+15(12)%2C+1553-60.

Stehman FB, Ali S, Keys HM, et al. Radiation therapy with or without weekly cisplatin for bulky stage 1B cervical carcinoma: Follow up of a Gynecological Oncology Group trial. *Am J Obstet Gynecol*. 2007; 197:1-6. doi: 10.1016/j.ajog.2007.08.003.

Vale C, Tierney JF, Stewart LA, et al. Reducing uncertainties about the effects of chemoradiation for cervical cancer: A systematic review and meta-analysis of individual patient data from 18 randomized trials. *J Clin Oncol*. December 2008; 26(35):5802-5812. doi: 10.1200/JCO.2008.16.4368.

Van Dyk S, Bernshaw D. Ultrasound-based conformal planning for Gynaecological Brachytherapy. Journal of Medical Imaging and Radiation Oncology. 2008; 52(1):77-84. doi: 10.1111/j.1440-1673.2007.01917.x.

Reviewed / Approved by  Patrick Browning, VP, Medical Director