



## 2007 QRRO Clinical Performance Measures (CPM)

### Radiation Oncology –Cervical Cancer

**Measure #C\_CM1:** Delivery of a biologically equivalent dose to Point A of 85 Gy +/- 5 % to patients with IB2-IVA cervical cancer treated with definitive irradiation

**Type of Measure:** This measure is appropriately used as a quality improvement measure.

Clinical Performance Measure
<b>Quantifiable Measure:</b> Percentage of patients with cervical cancer receiving definitive irradiation who receive a biologically equivalent dose of 85 Gy +/- 5% to Point A
<b>Numerator:</b> Patients with cervical cancer receiving definitive irradiation who receive a biologically equivalent dose of 85 Gy +/- 5% to Point A
<b>Denominator:</b> Patients with cervical cancer receiving definitive irradiation
<b>Denominator exclusions:</b> Medical comorbidities
<b>Rationale for the measure:</b> A basic tenant of radiation is that as tumor size increases, the dose of radiation necessary to control it must also increase. Cure of cervical cancer cervix requires a combination of external beam and brachytherapy to achieve doses in excess of traditional whole pelvis doses . There is some retrospective data to suggest a dose/response relationship. Eifel et al explored the relationship between brachytherapy dose and outcome in patients with bulky endocervical carcinomas treated with definitive irradiation. Patients who received < 6000 mg-hr had a higher rate of pelvic disease recurrence at 5 years as well as a decreased actuarial survival at 5 years than those patients who received > 6000 mg-hr (> 85-90 Gy). Among those who received > 6000 mg-hr, there was no significant relationship between brachytherapy dose and pelvic disease control. (1) In a study by Perez et al of definitive irradiation, in all stages except IB, higher doses of radiation delivered to the medial and lateral parametria with a combination of external beam and implant were correlated with a lower incidence of parametrial failures (< 60 Gy vs 60-90 Gy vs > 90 Gy to the medial parametria).(2)
<b>The following clinical recommendation statements are quoted verbatim from the referenced clinical guidelines and represent the evidence base for the measure:</b> Coia et al in the Patterns of Care analysis demonstrated a significantly higher survival rate and lower pelvic failure rate for patients who received a total dose of more than 65 Gy to the paracentral point. (3,4) A follow-up study by Montana et al concluded that the highest local control rate and disease-free survival are achieved with a total average paracentral dose of 75-85 Gy. (5) A dose-response relationship for in-field pelvic control, however, could only be documented in Stage III disease with the highest rate of pelvic control with paracentral doses > 85 Gy. (6,7)The NCCN guidelines recommend a combination of pelvic irradiation and brachytherapy to bring the point A dose to $\geq$ 85Gy.(Category 2A)
<b>QRRO Survey Form Questions:</b> I1 - 374, 401, 413, 421, 427, 431, 437, 441, 447, 451, 457, 461, 467, 500, 506, 516&517; 526&527; 536&537; 563&564; 573&574; 583&584; 593&594; 603&604; 613&614; 623& 624; 633&634; 643&644; 653&654; 663&664; 673&674; 735-746

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### References

1. Eifel PJ, Thoms WW, Smith TL, Morris M, Oswald MJ. The relationship between brachytherapy dose and outcome in patients with bulky endocervical tumors treated with radiation alone. *Int. J. Rad. Oncol. Biol. Phys.* 28:113-118, 1993.
2. Perez CA, Breaux S, Madoc-Jones H, Bedwinek JM, Camel HM, et al. Radiation therapy alone in the treatment of carcinoma of the uterine cervix I. analysis of tumor recurrence. *Cancer* 51:1393-1402, 1983.
3. Coia L, Won M, Lanciano R, Marcial VA, Martz K, et al. The patterns of care outcome study for cancer of the uterine cervix. *Cancer* 66:2451-2456, 1990.
4. Hanks GE, Herring DF, Kramer S. Patterns of care outcome studies results of the National Practice in Cancer of the Cervix. *Cancer* 51:959-967, 1983.
5. Montana GS, Martz KL, Hanks GE. Patterns and sites of failure in cervix cancer treated in the USA in 1978. *Int. J. Rad. Oncol. Biol. Phys.* 20:87-93, 1991.
6. Lanciano RM, Won M, Coia LR, Hanks GE. 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. Rad. Oncol.*
7. Lanciano R, Martz K, Coia L, et al. Tumor and treatment factors improving outcome in stage IIIb cervix cancer. *IJROBP* 20(1): 95-100; 1991.
8. NCCN guidelines 2008

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### Radiation Oncology –Cervical Cancer

**Measure #C\_CM2:** Use of brachytherapy in the definitive management of cervical cancer

**Type of Measure:** This measure is appropriately used as a quality improvement measure.

Clinical Performance Measure
<b>Quantifiable Measure:</b> Percentage of patients receiving definitive irradiation for cervical cancer who receive brachytherapy as part of their definitive treatment
<b>Numerator:</b> Patients receiving definitive irradiation for cervical cancer who receive brachytherapy as part of their definitive treatment
<b>Denominator:</b> All patients receiving definitive irradiation for cervical cancer
<b>Denominator exclusions:</b> Medical comorbidities
<b>Rationale for the measure:</b> Brachytherapy is essential in the definitive treatment of cervical cancer. The efficacy of brachytherapy is attributable to the ability of radioactive implants to deliver a higher concentrated dose more precisely to tissues than external beam alone, which contributes to local control and survival. Additionally, surrounding healthy tissues such as the bladder and rectosigmoid are relatively spared due to the rapid fall-off of dose with distance, around the applicators.
<b>The following clinical recommendation statements are quoted verbatim from the referenced clinical guidelines and represent the evidence base for the measure:</b> When curative treatment is planned, patients with cervical carcinoma treated with definitive irradiation should receive a combination of external beam irradiation and brachytherapy. As revealed in the Patterns of Care Studies and the retrospective series of Perez et al, recurrences and complications are decreased when brachytherapy is used in addition to external beam (1-5) Use of an intracavitary implant was the single most important treatment factor in multivariate analysis for stage IIIB cervix cancer with respect to survival and pelvic control in the 1973 and 1978 PCS studies (6,7). Retrospective series with external beam alone have proven marginal outcomes with this approach.
<b>QRRO Survey Form Questions: I1 - 374, 401, 500, 735-746</b>

References

1. Logsdson M, Eifel P. FIGO IIIB Squamous cell carcinoma of the cervix: An analysis of prognostic factors emphasizing the balance between external beam and intracavitary radiation therapy. *IJROBP*; 43(4):763-775, 1999
2. Perez CA, Breaux S, Madoc-Jones H, Bedwinek JM, Camel HM, et al. Radiation therapy alone in the treatment of carcinoma of the uterine cervix I. analysis of tumor recurrence. *Cancer* 51:1393-1402, 1983.
3. Coia L, Won M, Lanciano R, Marcial VA, Martz K, et al. The patterns of care outcome study for cancer of the uterine cervix. *Cancer* 66:2451-2456, 1990.
4. Lanciano RM, Won M, Coia LR, Hanks GE. 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. Rad. Oncol. Biol. Phys.* 20:667-676, 1991



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5. Montana GS, Martz KL, Hanks GE. Patterns and sites of failure in cervix cancer treated in the USA in 1978. Int. J. Rad. Oncol. Biol. Phys. 20:87-93, 1991.
6. Hanks GE, Herring DF, Kramer S. Patterns of care outcome studies results of the National Practice in Cancer of the Cervix. Cancer 51:959-967, 1983.
7. Lanciano R, Martz K, Coia L, et al. Tumor and treatment factors improving outcome in stage IIIb cervix cancer. IJROBP 20(1): 95-100; 1991.

## 2007 QRRO Clinical Performance Measures (CPM)

### Radiation Oncology –Cervical Cancer

**Measure #C\_CM3:** Completion of all radiation treatment in less than or equal to 60 days for patients treated for carcinomas of the intact cervix.

**Type of Measure:** This measure is appropriately used as a quality improvement measure.

Clinical Performance Measure
<b>Quantifiable Measure:</b> Percentage of patients with cervical cancer receiving definitive irradiation who complete treatment within <=60 days.
<b>Numerator:</b> Patients with cervical cancer receiving definitive irradiation who completed treatment within <=60 days
<b>Denominator:</b> All patients with cervical cancer receiving definitive irradiation
<b>Denominator exclusions:</b> None
<b>Rationale for the measure:</b> Optimal treatment duration for definitive irradiation should be ≤ 8 weeks. There is a demonstrated decrease in local control due to accelerated proliferation of tumor clonogens during radiotherapy with prolongation in overall treatment time (56, 99 ) Extending the overall treatment beyond 6-8 weeks can result in approximately a 0.5%-1% decrease in pelvic control and cause-specific survival for every extra day of overall treatment time.
<b>The following clinical recommendation statements are quoted verbatim from the referenced clinical guidelines and represent the evidence base for the measure:</b> Several retrospective analyses have suggested an adverse effect of prolonged treatment duration on outcome. The entire radiation course should be completed in a timely fashion(i.e. less than 8 weeks). The Patterns of Care study also documented a highly significant decrease in survival (p=.0001) and pelvic control (p=.0001) as the total time was increased from < 6, 6 to 7.9, 8 to 9.9, and > 10 weeks. Stage III accounted for the majority of the adverse effect from the prolongation of treatment time. When the analysis was performed by stage to evaluate the effect of overall treatment time with respect to the extent or bulk of disease, total treatment time continued to be an independent prognosticator for infield pelvic control and survival for stage III but not stages I and II. (115)
<b>QRRO Survey Form Questions: I1 - 374, 401, 413, 500, 504, 506, 769, 771, 773, 775, 777, 779, 781, 783, 785, 787, 789, 791, 793, 795, 797, 799</b>

References

1. Fyles A, Keane TJ, Barton M, Simm J. The effect of treatment duration in the local control of cervix cancer. Radiother. Oncol. 25:273-279, 1992.
2. Keane TJ, Fyles A, O'Sullivan B, Barton M, Maki E, et al. The effect of treatment duration on local control of squamous carcinoma of the tonsil and carcinoma of the cervix. Sem. Rad. Oncol. 2:26-28, 1992.
3. NCCN guidelines v1.2008



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4. Lanciano RM, Pajak TF, Martz K, Hanks GE. 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. Rad. Oncol. Biol. Phys.* 25:391-397, 1993.

## 2007 QRRO Clinical Performance Measures (CPM)

### Radiation Oncology –Cervical Cancer

**Measure #C\_CM4:** Use of Concurrent Cisplatin-containing chemotherapy with radiation

**Type of Measure:** This measure is appropriately used as a quality improvement measure

Clinical Performance Measure
<b>Quantifiable Measure:</b> Percentage of patients with cervical cancer receiving definitive irradiation who receive concurrent Cisplatin-containing chemotherapy
<b>Numerator:</b> Patients who receive concurrent cisplatin-containing chemotherapy with definitive irradiation
<b>Denominator:</b> All patients with cervical cancer receiving definitive irradiation
<b>Denominator exclusions:</b> Stage IA patients; Medical comorbidities
<b>Rationale for the measure:</b> The five prospective NCI trials reported in 1999 revealed a statistical survival advantage for patients who received concurrent chemotherapy with radiation vs those receiving radiation without chemotherapy. Most of these trails included the use of Cisplatin. Given the results of these five prospective trials this practice is considered the standard of care with a measurable survival advantage.
<b>The following clinical recommendation statements are quoted verbatim from the referenced clinical guidelines and represent the evidence base for the measure:</b> The NCCN panel reached a general agreement that radiation and concurrent cisplatin-based chemotherapy should be the treatment of choice for stages IIB, IIIA, IIIB, and IVA disease based on the results of the 5 randomized clinical trials. NCCN v.1.2008(Category 2A)
<b>QRRO Survey Form Questions: I1 - 151, 152, 153, 374, 401, 500, 683, 685, 686, 688, 690, 692, 735-746</b>

References

1. NCCN guidelines
2. Rose P, Bundy B, Watkins E, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *New England J of Med.* 340(15):1144-1153, 1999.
3. Keys H, Bundy B, Stehman F, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. *New England J of Med.* 340(15):1154-1161, 1999.
4. 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. *New England J of Med.* 340(15):1137-1143, 1999.
5. Peters III W, Liu P, Barrett II R, et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high risk early-stage cancer of the cervix. *Journal of Clinical Oncology*, 18(8):1606-1613, 2000.



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6. Whitney C, Sause W, Bundy B, et al. Randomized comparison of fluorouracil plus cisplatin vs. hydroxyurea as an adjunct to radiation therapy in stage II B-IVA carcinoma of the cervix with negative para-aortic lymph nodes: A Gynecologic Oncology Group and Southwest Oncology Group study. *Journal of Clinical Oncology* 17(5):1339-1348, 1999.

## 2007 QRRO Clinical Performance Measures (CPM)

### Radiation Oncology –Cervical Cancer

**Emerging Measure #C\_EM1:** Dosimetry with documentation of bladder, rectal and Point Adoses for each brachytherapy procedure performed in patients treated for cancer of the intact cervix

**Type of Measure:** This measure is appropriately used as a quality improvement measure.

<b>Clinical Performance Measure</b>
<b>Quantifiable Measure:</b> Percentage of patients with cervical cancer receiving definitive irradiation who have dosimetry with documentation of bladder, rectal, and Point A doses for each brachytherapy procedure.
<b>Numerator:</b> Percentage of patients with cervical cancer receiving definitive irradiation who have dosimetry with documentation of bladder, rectal and Point A doses for each brachytherapy procedure.
<b>Denominator:</b> Patients with cervical cancer receiving brachytherapy as part of their definitive irradiation
<b>Denominator exclusions:</b> None
<b>Rationale for the measure:</b> Inherent to gynecologic brachytherapy is the close proximity of the radioactive source(s) to the tumor and the normal pelvic organs. Documentation of tumor doses as well as the normal tissues doses is accomplished with image-guided computerized dosimetry. It is important to perform dosimetry for each radiation fraction even if the same applicator is used, as there may be quite a bit of variation in applicator position from fraction to fraction.(1,2,3,4,5,6) Additionally, there may be variation in the relationship of the applicator to the pelvic organs and applicator deformation of adjacent structures.(7) Variables which may impact on applicator position are vaginal packing, external applicator clamping, and the type of sedation/anesthesia used, as well as use of the dorsal lithotomy vs legs down position. The bladder and rectosigmoid may also change configuration due to changes in filling and doses may vary between fractions. Uterine and sigmoid mobility may also impact on the dose distribution. Additionally, disease regression and vaginal narrowing will vary from fraction to fraction and can also result in changes in dose distribution. A change in applicator can also result in changes in dose distribution as can changing the ovoid or ring size, ovoid separation, and tandem curvature. The ovoids may also change in separation and their relative position to the tandem over time as often times they are not fixed to the tandem.(3 4,5, 8) The applicator position relative to the pelvic organs is the most important factor in determining dose to these organs and this will vary from fraction to fraction.
<b>The following clinical recommendation statements are quoted verbatim from the referenced clinical guidelines and represent the evidence base for the measure:</b> Jones et al. found that when treatment planning was not performed for each fraction and only the initial dosimetry was used, there was increased dose to at-risk structures, such as the bladder and rectum.(5) Davidson et al found that a single dosimetric plan generated at the first fraction which was subsequently used for treatment of the remaining brachytherapy fractions without replanning resulted in significant increases in dose to the normal pelvic organs at risk. Treatment plans were recommended to be performed for each insertion to reflect current applicator and anatomical geometry.(9)
<b>QRRO Survey Form Questions: I1 - 374, 500, 504, 516-519, 526-529, 536-539, 550, 557, 563-566, 573-576, 583-586, 593-596, 603-606, 613-616, 623-626, 633-636, 643-646, 653-656, 663-666, 673-676</b>

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### References

1. Grigsby PW, Georgiou A, Williamson JF, Perez CA. Anatomic variation of gynecologic brachytherapy prescription points. *Int. J. Rad. Oncol. Biol. Phys.* 27:725-729, 1993
2. Hoskin PJ, Cook M, Bouscale D, Cansdale J. Changes in applicator position with fractionated high dose rate gynaecological brachytherapy. *Radiother. & Oncol.* 40:59-62, 1996.
3. Kim R, Meyer J, Spencer S, et al. Major geometric variation between intracavitary applications in carcinoma of the cervix: High dose rate vs. low dose rate. *IJROBP*;35(5):1035-1038, 1996.
4. Kim R, Meyer J, Plott W, et al. Major geometric variation between multiple high dose rate applications of brachytherapy in cancer of the cervix: Frequency and types of variation. *Radiology*; 195:419-422, 1995.
5. 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.
6. Pham H, Chen Y, Rouby E, et al. Changes in high-dose-rate tandem and ovoid applicator position during treatment in an unfixed brachytherapy system. *Radiology* 206:525-531, 1998.
7. Christensen G, Carlson B, Chao C, et al. Imaged-based dose planning of intracavitary brachytherapy: Registration of serial-imaging studies using deformable anatomic templates. *IJROBP*; 51(1):227-243, 2001.
8. Elhanafy O, Das R, Paliwal B, et al. Anatomic variation of prescription points and treatment volume with fractionated high-dose-rate gynecological brachytherapy. *Journal of Applied Clinical Medical Physics* 3(1):1-5, 2002
9. Davidson T, Yuen J, D'Souza D et al. Image-guided high-dose-rate brachytherapy treatment planning: Does Custom computed tomography planning for each insertion provides better conformal avoidance of organs at risk? *Brachytherapy* 7:37-42, 2008.

## 2007 QRRO Clinical Performance Measures (CPM)

### Radiation Oncology –Cervical Cancer

**Emerging Measure #C\_EM2:** Weekly documentation of hemoglobin levels in radiation therapy records

**Type of Measure:** This measure is appropriately used as a quality improvement measure

<b>Clinical Performance Measure</b>
<b>Quantifiable Measure:</b> Percentage of patients with cervical cancer receiving definitive concurrent chemoradiation who have weekly documentation of hemoglobin levels in the radiation therapy records during the course of the chemoradiation treatment
<b>Numerator:</b> Patients with cervical cancer receiving definitive concurrent chemoradiation who have weekly documentation of hemoglobin levels in radiation therapy records during the course of the chemoradiation treatment
<b>Denominator:</b> Patients with cervical cancer receiving definitive concurrent chemoradiation
<b>Denominator exclusions:</b> None
<b>Rationale for the measure:</b> Anemia at presentation is known to be a negative prognostic factor in patients with cervical cancer. (1) It is debated whether the detrimental effect of anemia is due to the associated hypoxia of this condition or reflects the burden of disease. Transfusion efficacy is debated. A study by Bush et al at Princess Margaret Hospital reported in 1986, demonstrated an improvement in pelvic disease control with the transfusion of anemic patients.(2) The results have never been duplicated in another study. In a later study by Fyles et al, transfusion during treatment was an adverse prognostic factor.(3) The relationships between hypoxia, transfusion and treatment outcome are complex and deserve further study. (4) Use of erythropoietin (Procrit) has not been found to improve outcome when given during radiation and has been associated with an increase in deep venous thrombosis. (4) In a review of 494 patients with advanced cervical carcinoma treated on two prospective GOG trials, hemoglobin levels in the last half of chemoradiation, rather than at diagnosis, were the most predictive of disease recurrence or survival. (5) Despite conclusive evidence that transfusion improves local control and survival, careful monitoring of blood counts during and after radiation is important as both the chemotherapy and radiation can be myelosuppressive. This may be poorly tolerated in elderly or frail patients. Depression of the blood counts is the most common side effect from chemoradiation. It is the primary reason that patients can often not complete their intended cycles of chemotherapy during radiation. Acute toxicities have varied among the trials and have been mostly hematologic or gastrointestinal, but acute toxicity appears tolerable. (7) With concurrent chemoradiation, there is certainly the potential for an increase in acute toxicity, and close monitoring is required during treatment with attention to blood counts and GI reactions. Additionally, there is the potential for treatment prolongation because of this toxicity, and this must be avoided. Serkies and Jassem analyzed 112 patients treated with concurrent cisplatin and radiation. Only 26% received a full and timely course of cisplatin. For 29%, the interval between cycles was prolonged and 55% did not receive the planned 5 cycles of cisplatin because of toxicity or compliance. (8) Interventions to minimize these compromises in therapy are important and begin with close monitoring of the blood counts on a weekly basis.

## 2007 QRRO Clinical Performance Measures (CPM)

The following clinical recommendation statements are quoted verbatim from the referenced clinical guidelines and represent the evidence base for the measure: Pending

QRRO Survey Form Questions: I1 - 10&11, 20&21, 30&31, 40&41, 50&51, 60&61, 70&71, 374, 375-378, 401, 683, 685

### References:

1. Werner-Wasik M, Schmid CH, Bornstein L, Ball HG, Smith DM, et al. Prognostic factors for local and distant recurrence in stage I and II cervical carcinoma. *Int. J. Rad. Oncol. Biol. Phys.* 32:1309-1317, 1995.
2. Bush R, The significance of anemia in clinical radiation therapy. *Int J Radiat Oncol Biol Phys* 12:2047-2050, 1986.
3. Fyles AW, Pintilie M, Kirkbride P, Levin W, Manchul LA, et al. Prognostic factors in patients with cervix cancer treated by radiation therapy: results of a multiple regression analysis. *Radiother. Oncol.* 35:107-117, 1995.
4. Fyles A, Milosevic M, Pintilie M, et al Anemia , hypoxia and transfusion in patients with cervix cancer: a review *Radiotherapy and Oncology* 57:13-19, 2000..
5. Winter III W, Maxwell GL, Tian C, et al. Association of hemoglobin level with survival in cervical carcinoma patients treated with concurrent cisplatin and radiotherapy: a Gynecologic Oncology Group study. *Gynecologic Oncology* 94:495-501, 2004.
6. Lavey R, Liu PY, Greer B, et al. Recombinant human erythropoietin as an adjuvant to radiation therapy and cisplatin for stage IIB-IVA carcinoma of the cervix: A Southwest Oncology Group Study. *Gynecologic Oncology* 95:145-151, 2004 .
7. Rose P. Combined-modality therapy of locally advanced cervical cancer. *Journal of Clinical Oncology*, 21(10s):211s-217s, 2003.
8. Serkies K, Jassem J. Concurrent weekly cisplatin and radiotherapy in routine management of cervical cancer: A report on patient compliance and acute toxicity. *Int J Radiation Oncol Biol Phys* 60(3):814-821, 2004.