



Advancing Research. Improving Lives.™

NRG ONCOLOGY PROTOCOL DEVELOPMENT TEMPLATE FOR RADIATION THERAPY

DISEASE SITE: Gynecological Cancer
SUB-COMPONENT: Endometrial Cancer (post-operative treatment
After hysterectomy)

Authors & Affiliations:

Yongsok C. Lee, Ph.D., Miami Cancer Institute, Baptist Health South Florida, Miami, FL
Hayeon Kim, Ph.D., University of Pittsburgh Medical Center, Pittsburgh, PA
Pingfang Tsai, Ph.D., New York Proton Center, New York, NY
Xiaoying Liang, Ph.D., Mayo Clinic, Jacksonville, FL
Kyle Padgett, Ph.D., University of Miami, Miami, FL
Lorraine Portelance, M.D., University of Miami, Miami, FL

Reviewers & Affiliations:

Stanley H. Benedict, Ph.D., University of California at Davis, Sacramento, CA
Jessica R. Lowenstein, M.S., UT MD Anderson Cancer Center, Houston, TX
Ivy A. Petersen, M.D., Mayo Clinic, Rochester, MN
Robert A. Price, Ph.D., Fox Chase Cancer Center, Philadelphia, PA
Ying Xiao, Ph.D., University of Pennsylvania, Philadelphia, PA
Anuja Jhingran, M.D., UT MD Anderson Cancer Center, Houston, TX
Hyejoo Kang, Ph.D., Loyola University Medical Center, Chicago, IL
Marina Sala, Ph.D., MBA, University of South Florida, Tampa, FL
Diandra Ayala-Peacock, M.D., Duke University, Durham, NC
Jay Shiao, M.D. MPH, University of Kansas Medical Center, Kansas City, KS

Maintained By: NRG Medical Physics Subcommittee
NRG Radiation Oncology Committee

Version 1: 05-2024

This protocol template was designed and developed by NRG Oncology. It is intended to be used only in conjunction with an IRB approved study. No other use or reproduction is authorized by NRG Oncology nor does NRG Oncology assume any responsibility for unauthorized use of this template



Text that is both underlined and highlighted is either an instruction or a suggestion to be deleted or replaced by the Principal Investigators (PIs) using regular text.

Text that is highlighted but not underlined is an example to be selected (by removing the highlighting), deleted or replaced by the PIs using regular text.

5.2 Radiation Therapy

This section should clearly describe the modality used to deliver radiation, the method for patient immobilization, and the prescribed dose. Requirements for any applicable credentialing (including phantom irradiation credentialing, image-guided radiation therapy (IGRT) credentialing, brachytherapy credentialing, positron emission tomography (PET)/computed tomography (CT) scanner credentialing, and dry run & pre-treatment review should be explicitly specified in the protocol.

Notes 1,2,...: The note(s) included at this point in the protocol should emphasize special information that the study chair does not want the investigator to overlook. An example is a statement that IGRT is required for the study.

5.2.1 Treatment Technology

List the allowed treatment modalities including the technique and the energy (e.g. photons, protons, electron, brachytherapy, etc.) along with the required capabilities (e.g. intensity modulated radiation therapy (IMRT), IGRT, on-board adaptive IMRT, etc.).

External Beam Radiation Therapy (EBRT)

Photon Therapy

Radiation therapy can be delivered via 3D-conformal radiation therapy (3D-CRT) or IMRT targeting upper vagina and pelvic nodes. 3D-CRT plans can be a 4-field box arrangement or other field arrangements. IMRT plans may include static field arrangements (e.g. 5-9 fields), volumetric modulated arc therapy (VMAT), or TomoTherapy. A pseudo-step-wedge intensity modulation (PSWIM) technique is permitted. MR guided treatment is allowed if a maximum field size can cover the entire target area. The two active MR guided treatment options (Viewray and Elekta) have smaller field sizes than conventional Linacs: 27.4 cm × 24.1 cm for Viewray and 57.4 cm × 22.0 cm for Elekta. Also, the use of on-table adaptive techniques, either CBCT or MRI based is permitted. These adaptive techniques can better account for inter-fraction motion which results in reduced margins and potentially better OAR sparing. 3D-CRT should use 4-18 MV photons and for IMRT, 6-10 MV photons are recommended.

If MR-guided RT is used in the protocol, guidance should be provided as to when on-board adaptive RT should/could be used (for example during the boost delivery, an isotoxic approach is recommended).

Proton Therapy

A cyclotron or synchrotron-based proton therapy machine must be equipped at least with orthogonal

kV x-ray imaging. In-room 3D volumetric imaging capabilities are preferable to monitor anatomical changes. Continuous variable or discrete energies of 70-230 MeV are allowed. The proton energies used for each field should be based on the range and spread-out Bragg peak (SOBP) that is suitable to cover the treatment volume. Double-scattering, uniform scanning, wobbling or intensity-modulated proton therapy (IMPT) using pencil beam scanning is considered an acceptable proton treatment technique. The range shifter is applied when treating shallow target depths.

Brachytherapy

Vaginal cuff brachytherapy can be delivered without EBRT or as a boost. High dose rate (HDR), pulsed dose rate (PDR) or low dose rate (LDR) is permitted. Dose optimization should be used in an effort to create reasonable homogeneity of dose around the surface of the applicator. A vaginal length of 3-5 cm (length of the relevant isodose) can be treated at the discretion of the radiation oncologist.

5.2.2 Immobilization and Simulation

Immobilization

Describe the recommended patient setup and immobilization methods.

EBRT

Photon/Proton Therapy

Patients are to be immobilized in the supine or prone position in an immobilization device. Immobilization should be performed to ensure the pelvis is positioned consistently throughout treatment. This can be accomplished by immobilizing legs with a custom cradle such as a vac-loc, or a non-custom device such as a med-tec. If an MR-Linac is to be used for treatment the immobilization equipment utilized needs to be MRI-compatible.

Proton Therapy

Immobilization devices for proton therapy patients should also be chosen such that the daily setup errors, both translation and rotational, would cause minimal beam range variations through these devices. All the immobilization devices used in the simulation should be commissioned with appropriate proton-stopping power. An excessive amount of immobilization device should not be in the beam path. Prior to the simulation, a water filled rectal balloon could be inserted to minimize air and increase vaginal location stability. Proper customized immobilization and assessment and, if necessary, management of internal motion are essential for effective treatment. The skin fold should be carefully assessed if there is a potential to be in the proton beam path. The variations due to daily differences of patients settling into the immobilization devices should be minimized.

Brachytherapy

Patients are in the supine position with the vaginal applicator in place.

Simulation Imaging

This subsection should include information about the extent of CT or MRI imaging, the resolution of the scan including the slice thickness, and details of the allowed/suggested use of contrast agents and

the handling of tissue densities when contrast is used.

EBRT

Photon/Proton Therapy

Prior to simulation, radio-opaque marker seeds or clip(s) may be inserted into the vaginal apex to help identify the area by CT scan. Vaginal markers which distend the vagina are not recommended. Moderate bladder filling is encouraged for simulation and treatment to reduce the small bowel treated. A CT simulation scan is required with a slice thickness ≤ 3.0 mm to define clinical target volume (CTV) and planning target volume (PTV). The scan regions should be extended from L1 to mid-thigh. One scan should be obtained with the bladder full and one with the bladder empty. These scans will be fused to contour the vaginal internal target volume (ITV). IV contrast and bowel prep-contrast are allowed for better delineation of the contrast enhanced pelvic vessels and small bowel contouring. If contrast material is used, the scans are performed without and with contrast. The scan without contrast is to be used for planning. If only one scan with contrast is obtained, the contrast should be overridden with a density of soft tissues for treatment planning. For patients treated with a MR-Linac system a planning MRI will also be done and the planning CT scan should be performed with the same immobilization and patient positioning to facilitate electron density migration to the MRI planning dataset if necessary. The planning MRI could be done either using a formal planning MRI unit or in the MR-Linac system. Additional quality assurance and correct sequence selection are needed to ensure an accurate whole-body contour is available for planning as geometrical uncertainties are increased at the edge of the MRI imaging field

Brachytherapy

Patients are simulated with brachytherapy applicators in place with kV AP images, CT or MR imaging. The images should contain the entire brachytherapy applicators and critical structures including the bladder, rectum, bowel and vagina. Vaginal marker seeds or clips can be used to verify that the applicator is in contact with the vaginal mucosa, especially if kV is the imaging modality chosen.

Motion Management Technique

Please remove this subsection if it does not apply to your protocol.

EBRT

The motion of the vagina with bladder filling should be taken into consideration in defining the vaginal ITV. Patients should be simulated with a full and empty bladder to evaluate vaginal motion. Ideally treatment planning should be performed on the full bladder scan and patients should be treated with a full bladder. If on-table adaptive RT, either MRI or CBCT based, is to be delivered then the use of an ITV may not be necessary and expansions from the CTV don't need to account for inter-fractional motion.

Verification imaging or ultrasound to evaluate bladder filling is allowed but not required as long as an ITV is created to ensure that the vagina will be within the vaginal ITV regardless of daily bladder filling status. Treatment with full bladder will help to reduce the volume of bowel treated and should thus be encouraged. Although on-board adaptive RT provides the opportunity to adapt to the anatomy of the day, it is desirable to maintain bladder filling consistency as much as possible.

Creating several different plans that account for different anatomical situations (i.e., empty bladder/full bladder, anteverted/retroverted uterus, etc...) and performing daily imaging to decide which plan from the library of plans is best suited for the day is another valid approach to deal with inter-fraction motion. This efficient approach has the advantage of addressing inter-fraction motion without the need for daily on-board adaptation.

Brachytherapy

A fixation device may be used to minimize applicator rotation and cephalon-caudal motion during treatment.

5.2.3 Imaging for Structure Definition, Image Registration/Fusion and Follow-up

Please remove this subsection if it does not apply to your protocol.

EBRT

Photon/Proton Therapy

Diagnostic Pelvic MRI and/or PET-CT fusion with the CT/MRI simulation scan is recommended to aid target delineation. Ideally the diagnostic MRI should be done immediately before or after the planning CT/MRI scan. Fusion should be optimized to match the diagnostic MRI/PET-CT scans to the treatment position. Rigid/deformable image registration between PET-CT and CT/MRI simulation scans can be performed and should be reviewed with caution. Deformable image registration between diagnostic MRI and CT/MRI simulation scans is not encouraged to avoid deforming the tumor. For MR-guided treatment, the diagnostic studies should be fused to the planning MRI.

5.2.4 Definition of Target Volumes and Margins

Note: All structures must be named for digital RT data submission as listed in the table below. The structures marked as “Required” in the table must be contoured and submitted with the treatment plan. Structures marked as “Required when applicable” must be contoured and submitted when applicable. Resubmission of data may be required if labeling of structures does not conform to the standard DICOM name listed. Capital letters, spacing and use of underscores must be applied exactly as indicated.

Entries in the first column of the list below will be entered and edited by the QA Staff. The PIs are required to specify the information in the second and third columns. The detailed specifications have to include crucial items such as boundary definitions and margins.

EBRT

Standard name	Description	Validation Required/Required when applicable/Optional
GTV	GTV to receive cGy	Required
CTV	CTV to receive cGy	Required

ITV_	ITV to receive cGy	Contour is required only when ITV approach is used.
PTV_	PTV to receive cGy	Required (Photon only)

Detailed Specifications

Please refer to the *RTOG Gynecological Atlas for volume specification*. The atlas may be accessed on the RTOG website at: <https://www.rtog.org/CoreLab/ContouringAtlases/GYN.aspx>

GTV_: For post-operative patients with no gross disease, there should not be a gross tumor volume (GTV). Patients with residual nodal disease will have a nodal GTV.

CTV_: CTV_ composed of the vaginal CTV and nodal CTV.

Vaginal ITV: The vaginal ITV is an expansion of the vaginal CTV which includes the upper half of the vagina as well as the paravaginal tissues that extend from the vaginal apex (or soft tissues of 0.5-2cm above the vaginal radio-opaque marker) to the obturator muscle. The vaginal CTV should be contoured on the full bladder scan. The vaginal CTV should then be expanded to account for vaginal motion by evaluating the position of the vaginal apex on the bladder empty scan. If gas/stool distends the rectum, the CTV is to be expanded to include the anterior half of the rectum to account for evacuation of the rectum. The final vaginal ITV volume will include the posterior wall of the bladder and may include anterior wall of the rectum, and external iliac lymph node regions (<https://www.nrgoncology.org/ciro-gynecologic>). Bone and muscle should be excluded from the nodal CTV. Small bowel may be included if it falls within the nodal CT volume. The nodal CTV will include at least 7 mm margin around the vessels. Approximately 1-2 cm of tissue anterior to the sacrum (S1-S3) may be added to the CTV for adequate coverage of presacral nodes at the discretion of the treating physician (in protocol, the PIs should indicate when treatment of the presacral nodal region is appropriate). In addition, the most antero-lateral margin of the external iliac nodes that lie just proximal to the inguinal canal should be excluded from the CTV (nodal CTV should stop at the femoral head). The nodal CTV should end 7 mm from the L4-5 to L5-S1 interspace.

PTV_: PTV_ should be created by expanding the CTV or ITV volume by 5-7 mm in all dimensions. When using on-board adaptive RT approaches the appropriate margins utilized may be reduced but need to be fully evaluated as each approach has different efficacies in dealing with inter and intra-fraction motion (Plan Library, CBCT Guided, real-time tracking and MRI Guided) (Photon only)

For proton therapy, only CTV is defined as the treatment target, and robustness optimization shall be applied to the CTV to ensure coverage. Much like the PTV is a surrogate to ensure proper CTV coverage in photon therapy, a robustness analysis must be used to verify appropriate CTV coverage for proton treatment.

5.2.5 Definition of Critical Structures and Margins

Note: All structures must be named for digital RT data submission as listed in the table below. The structures marked as “Required” in the table must be contoured and submitted with the treatment plan. Structures marked as “Required when applicable” must be contoured and submitted when applicable. Resubmission of data may be required if the labeling of structures does not conform to the standard DICOM name listed. Capital letters, spacing and use of underscores must be applied exactly as

indicated.

Entries in the first column of the list below will be entered and edited by the QA Staff. The PIs are required to specify the information in the second and third columns. The detailed specifications have to include crucial items such as boundary definitions and margins.

EBRT

Photon Therapy

Standard name	Description	Validation Required/Required when applicable/Optional
External	External patient contour	Required when applicable
External-PTV	All tissues excluding the PTV	Required when applicable
Spc_Bowel	The space that the bowel may occupy	Required
Rectum	Rectum	Required
Bladder	Bladder	Required
Femur_L	Left femur	Required
Femur_R	Right femur	Required
BoneMarrow	Bone Marrow	Optional

Proton Therapy

Standard name	Description	Validation Required/Required when applicable/Optional
External	External patient contour	Required when applicable
External-CTV	All tissues excluding the CTV	Required when applicable
Spc_Bowel	The space that the bowel may occupy	Required when applicable
Rectum	Rectum	Required
Bladder	Bladder	Required
Femur_L	Left femur	Required
Femur_R	Right femur	Required
BoneMarrow	Bone Marrow	Optional

Detailed Specifications

Photon/Proton Therapy

Spc_Bowel: Small bowel will be contoured in each slice in which it appears including at least 2 cm but no more than 3-4 cm above the PTV (photon) or CTV (proton). The small bowel will be contoured in its entirety within these parameters, including adipose and mesentery.

Rectum: Rectum will be contoured in each slice in which it appears. As a general guideline, the radiation oncologist can consider the maximum caudal extent of the rectum to lie 1.5-2.0 cm from the bottom of the ischial tuberosities. Superiorly, judgment will be required to establish where the rectum ends and the sigmoid colon begins. The transition to the sigmoid colon is marked by increased curvature and tortuosity in its path.

The outer rectal wall will be contoured and filled in, treating the organ as a solid continuous structure, and will be defined from the level of the sigmoid flexure to the anus.

Bladder: Bladder will be contoured in each slice in which it appears. The outer bladder wall will be contoured and filled in, treating the organ as a solid continuous structure.

BoneMarrow: The pelvic bone will be contoured as a surrogate for the bone marrow. The pelvic bone from the superior to the inferior aspect of the PTV (photon) or CTV (proton) can be auto-contoured. This can be accomplished with the use of a CT-density-based auto-contouring algorithm. The femoral heads but not the femoral necks should be included in the bone marrow contour.

5.2.6 Dose Prescription

Note: The information provided in this section can be used for adjusting the dose constraints for treatment planning purposes. This table, together with the planning priority table, should be used during dose optimization. It is important to remember that ideal plans might not be achievable in all cases. Thus, the Compliance Criteria table could be different than the information given here. Cases will be scored using the Compliance Criteria table.

EBRT

Photon Therapy

Target standard name	Dose (Gy)	Fraction size (Gy)	# of fractions	Frequency	Dose specification technique
CTV_4500	45	1.8	25	Daily	Covering 99% of CTV
PTV_4500	45	1.8	25	Daily	Covering 95% of PTV
CTV_5040	50.4	1.8	28	Daily	Covering 99% of CTV
PTV_5040	50.4	1.8	28	Daily	Covering 95% of PTV

Proton Therapy

Robustness optimization to the CTV is recommended for proton therapy, with setup uncertainties (the same as the PTV margin) in all directions. Range uncertainties should be used according to their institutions' protocol.

Brachytherapy boost (EBRT Photon + brachytherapy)

HDR

Total EBRT (Gy)	HDR dose/fraction (Gy)	No. of HDR fractions	Dose specification point	Total HDR dose (Gy)	Total EQD2Gy(10) (Gy)
45	5.0-6.0	2-3	0.5 cm depth	10-18	56.8-68.3
45	5.0	2	Surface	10	56.8
50.4	5.0-6.0	2	0.5 cm depth	10-12	62.1-65.6
50.4	5.0	2	Surface	10	62.1

where EQD2Gy(10) = Total Biological Equivalent Dose in 2 Gy Fractions for tumor effects ($\alpha/\beta=10$)

PDR/LDR

Total EBRT (Gy)	PDR/LDR dose/fraction (Gy)	No. of PDR/LDR fractions	Dose specification point	Total PDR/LDR dose at vaginal surface (Gy)	Total dose at vaginal surface (Gy)
45	25	1	Surface	25	70
50.4	25	1	Surface	25	75.4

Brachytherapy alone

HDR

HDR dose/fraction (Gy)	No. of HDR fractions	Dose specification point	Total HDR dose (Gy)
7.0	3	0.5 cm depth	21
6.0	5	Surface	30
4.0	6	Surface	24

PDR/LDR

PDR/LDR dose/fraction (Gy)	No. of PDR/LDR fractions	Dose specification point	Total PDR/LDR dose (Gy)
60	1	Surface	60

5.2.7 Compliance criteria

The compliance criteria listed here will be used to score each case. Given the limitations inherent in the treatment planning process, the numbers given in this section can be different than the prescription table. The Per Protocol and Variation Acceptable categories are both considered to be acceptable. The Per Protocol cases can be viewed as ideal plans, and the Variation Acceptable category can include more challenging plans that do not fall at or near the ideal results. A final category, called Deviation Unacceptable, results when cases do not meet the requirements for either Per Protocol or Variation Acceptable. Plans falling in this category are considered to be suboptimal and additional treatment planning optimization is recommended.

VxGy[cc], VxGy[%], Vx%[cc], Vx%[%]: Volume [cc or %] receiving Dose or higher [Gy or %]
 Dxcc[Gy], Dxcc[%], Dx%[Gy], Dx%[%]: Dose [Gy or %] to Volume [cc or % of total volume]
 Minimum dose is defined to D98%[Gy] or D98%[%]
 Maximum dose is defined as D0.03cc[Gy] or D0.03cc[%]
 Mean[Gy] or Mean[%]: Mean dose in Gy or %

Normalization of Dose: The plan is normalized such that 95% of the PTV_ volume receives 95% of prescription dose or higher.

Note: Deviation Unacceptable occurs when dose limits for Variation Acceptable are not met

Target Volume Constraints and Compliance Criteria

EBRT

Photon Therapy

Name of structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Notes (Please remove this column when notes are not needed)
CTV_4500	D99% [% of PD]	>=99	>=95	
PTV_4500	D95% [% of PD]	>=95	>=90	
	D0.03cc [% of PD]	<=110	<=115	
CTV_5040	D99% [% of PD]	>=99	>=95	
PTV_5040	D95% [% of PD]	>=95	>=90	
	D0.03cc [% of PD]	<=110	<=115	

Per Protocol range is excluded from Variation Acceptable range. PD = prescribed dose

Proton Therapy

Robustness analysis of any proton treatment plan should account for, at a minimum, eight positional offset scenarios (plus/minus in each direction) and range independently. The value for the position should be similar to the photon's PTV margin (e.g., 3-5 mm), and the range should be the standard value for the institution (e.g., 3-5%). The margin defined here is as water equivalent distance (WED), not the geometric expansion from the CTV. The beam-specific proximal or distal margins are calculated from the CTV based on the range and the SOBP of the specific beam. The lateral margin considers a setup error of 3-5 mm plus the additional margin required to cover the CTV (e.g., penumbra (passive scattering) or one spot sigma (pencil beam scanning)). For target coverage dose constraints of proton plans, the values reported must be obtained from the worst-case scenario of the robustness analysis.

Normal Structure Constraints and Compliance Criteria

EBRT

Photon Therapy (IMRT)

Note that constraints may be changed depending on variations in the protocol.

Name of structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Notes (Please remove this column when notes are not needed)
Rectum	V40Gy [%]	<=80	<100	
Bladder	V45Gy [%]	<=35	<70	
Spc Bowel	V40Gy [%]	<=30	<70	
Femurs	D15% [Gy]	<=30	<=50	
	D0.03cc [Gy]	<=50	<=55	
BoneMarrow (if applicable)	Mean [Gy]	<=27	<=29	
	V10Gy [%]	<=90	V25Gy <90%	
	V40Gy [%]	<=37	<60	

Per Protocol range is excluded from Variation Acceptable range.

Proton Therapy

For OAR dose parameters (excluding _PRV structures) of proton plans, the dose parameters should be reported from the nominal plan only. For OAR that are defined with a _PRV of proton plans, the dose parameters should be obtained for the worst-case scenario of the robustness evaluation on the nominal structure contour (not the expanded _PRV structure).

Delivery Compliance criteria

	Per Protocol	Variation Acceptable	Notes (Please remove this column when notes are not needed)
Start date (X days/weeks after X) (Please remove this row when the start date is not specified in the protocol.)	4-9 weeks after surgery	4-12 weeks after surgery	
Treatment delays	Interruption of 0 days	Interruption of 1-7 consecutive days	
Overall treatment time	<=50* days	<=56 days	

*For a patient receiving 28 fractions, the course of treatment would be 38 days, 50 days would be more than 7 days of delay, therefore should not be listed as per protocol.

5.2.8 Treatment Planning Priorities and Instructions

- Critical Structure and Target priorities must be listed in order of decreasing importance (We may also use one importance factor for a group of structures).

The following list is an example

EBRT

1. PTV (photon)/CTV (proton)

2. Spc_Bowel
3. Rectum
4. Bladder
5. Femurs
6. BoneMarrow (if applicable)

If max dose constraints are exceeded, the following solution can be entertained:

For 3D-CRT, use the field in field technique to decrease hot spots and to reduce the bowel dose.

- Required algorithms

(Convolution/Superposition, Monte Carlo, etc...)

For Convolution/Superposition-type algorithms, the dose should be reported as computed inherently by the given algorithm. For Monte Carlo or Grid Based Boltzmann Solver algorithms, conversion of D_m (dose-to-medium) to D_w (dose-to-water) should be avoided. D_m , computed inherently by these algorithms, should be reported.

- Primary dataset for dose calculation

EBRT

Photon Therapy

The primary data set for dose calculations is CT. In the case in which contrast is present during the treatment planning CT, the density of the contrast should be overridden to a representative background electron density. Heterogeneity corrections must be applied. For MRI-guided EBRT treatments the primary dataset will often be a planning MRI, but to utilize planning MRI datasets for treatment planning the imaging system and workflows must be properly commissioned. Additionally, MRI simulators now exist that can create electron density maps so that a planning MRI can be utilized for dose calculations. Again these imaging systems and workflows need to be properly commissioned prior to use.

Proton Therapy

The Monte Carlo algorithm for optimization is highly recommended. If the Monte Carlo optimization is not used, at least the Monte Carlo calculation dose should be calculated as a reference.

Brachytherapy

Planning can be performed on CT or utilizing library plans with dose points reported to the prescription depth (cylinder surface or 0.5 cm). Dose points should be reported along the length of the cylinder at the patient right and left at 2 cm increments. For example, patients treated to the upper 3 cm of the vagina should report dose to the cylinder surface along the cylinder surface at 2 cm from the dome apex. For homogeneous dose distributions, ideally, points along the applicator or 0.5 cm from the applicator are within 10% of the prescription dose. kV AP images or planning CT images can be provided. Heterogeneity corrections are not mandatory. Volumetric dose constraints do not need to be reported for brachytherapy cases, given the low rates of toxicity with cuff and the lack of evidence of dose constraints in vaginal cuff brachytherapy treatment. Instead, verification of the optimal position of the dome in the vagina with CT or an AP film is highly recommended, as well as reporting of dose homogeneity along the cylinder.

- Dose matrix resolution

Dose grid size should be ≤ 3 mm (preferably ≤ 2 mm to minimize effects of partial volume averaging)

in all directions.

- List treatment planning recommendations and give link to FAQs

5.2.9 Patient specific QA

- Describe the technique and give the Gamma Index Analysis pass rate recommendation

For photon IMRT/VMAT plans or proton IMPT plans, patient-specific QA is highly recommended. Any patient-specific QA performed should follow respective institutional guidelines. If on-table adaptive RT is to be performed, then patient-specific QA is also recommended. The recommended patient specific QA criterion is that 90% of the comparison points pass gamma criteria of dose difference/distance-to-agreement of $\pm 3\%/2$ mm with a 10% dose threshold (AAPM TG 218 report).

5.2.10 Daily Treatment Localization/IGRT

Image-guided radiation therapy (IGRT) is radiation therapy using imaging to facilitate accuracy and precision throughout its entire process, from target and normal tissue delineation, to radiation delivery, to adaptation of therapy to anatomic and biological changes over time in individual patients. In this section we use the terminology IGRT to focus on image-guidance at the time of radiation delivery to ensure its adherence to the planned treatment.

If the protocol requires IGRT, the following information should be provided for localization guidance

- Will simple isocenter localization technique be used at the beginning of treatment and weekly thereafter?
- Will more advanced IGRT techniques be used?
- Is IGRT tied to margin reduction?
- Allowed image guidance methods: 2D x-ray, 3D x-ray, electromagnetic localization, optical surface imaging, MRI-guidance, other
- Image registration techniques: fiducial markers, bone as surrogate, soft tissue, other
- State the frequency for localization checks
- Give recommendations for correcting (e.g. correcting for linear shifts less than 1 cm is not recommended)
- Recording of shift information must be provided for the IGRT credentialing process
- Other

EBRT

Daily IGRT is required for this protocol when the IMRT or IMPT treatment technique is used. Any form of online imaging is acceptable, such as MV or kV planar imaging, MVCT or MV CBCT, kV CBCT, CT on rails, on board MRI, etc. The AAPM recommendations for verifying the coincidence of the imaging and treatment reference points must be adhered to the daily use of IGRT. At the time of simulation, it is recommended to place the isocenter along the patient's midline 1.5 cm caudal to the inferior border of the sacroiliac joint. In general, the CT or CBCT/on board MRI will be used for setup verification using bone landmarks only and not for soft tissue alignment. Small soft tissue shifts may be acceptable. Otherwise, the treating physician may elect to postpone treatment or re-simulate (not if an ITV is used).

Brachytherapy

Daily imaging is not required but recommended for applicator position verification.

Management of Radiation Dose to the Patient from IGRT

NRG Oncology is concerned about the estimated doses given from IGRT, and is committed to limiting the imaging dose when IGRT is used in any of its protocols. This can be accomplished by avoiding the use of this technology to make small changes in patient positioning that are within the stated PTV margins. The imaging dose to the patient may become significant if repeated CBCT studies are performed for patients with severe set up problems (e.g. requiring frequent corrections that are larger than the PTV margins). It is recommended that patients demonstrating severe set-up problems during the first week of treatment be moved to a treatment with larger margins or be re-simulated. MRI guidance strategies are beneficial in the management of radiation dose from IGRT due to the fact that no-ionizing radiation is used to generate these high-quality on-board images.

5.2.11 Case Review

A group of radiation oncologists will perform ongoing remote RT Quality Assurance Review after EBRT and brachytherapy cases enrolled have been received at IROC Philadelphia and IROC Houston respectively.