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NRG ONCOLOGY PROTOCOL DEVELOPMENT TEMPLATE FOR RADIATION THERAPY

DISEASE SITE: Gynecological Cancer

SUB-COMPONENT: Cervix, Uterine Cervix

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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

Pelvis

Pelvis radiotherapy can be delivered via 3D-conformal radiation therapy (3D-CRT) or IMRT. 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), modulated arc therapy, or TomoTherapy. A pseudo-step-wedge intensity modulation 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.

Parametrial and/or Nodal Boost

A parametrial boost and/or a nodal boost can be delivered at the treating physician's discretion, and it can be accomplished via 3D-CRT or IMRT sequentially, or IMRT as a simultaneous integrated boost (SIB). In the context of parametrial and/or nodal boost (dose escalation) an on-board adaptive approach has the advantage of plan adjustments to protect the luminal organs.

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

High dose rate (HDR), pulsed dose rate (PDR) or low dose rate (LDR) brachytherapy is permitted. Either standard (point-directed) or volume-directed brachytherapy techniques are permitted according to each institution's standard. Volume-directed brachytherapy is encouraged with MRI-based volumetric brachytherapy preferred when feasible. Intracavitary (e.g., tandem and ovoids, or tandem and ring) and/or hybrid or template-based interstitial (e.g., interstitial applicators) brachytherapy is permitted. Brachytherapy is the standard of care to boost the central disease after a course of pelvic EBRT, but in certain cases where patients are poor candidates for brachytherapy, on-board MRI adaptive EBRT might be an option.

5.2.2 Immobilization and Simulation

Immobilization

Describe the recommended patient setup and immobilization methods.

EBRT

Photon/Proton Therapy

Patients can be simulated in the supine or prone position. All subjects should have a customized immobilization device (supine) or a bowel exclusion device (prone) fabricated at the time of simulation. For treatment for pelvis, legs are immobilized with a custom/non-custom device. For treatment for pelvis plus paraaortic lymph nodes, abdomen, pelvis, and legs are immobilized with a custom/non-custom device. 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. 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 brachytherapy applicators in place. For HDR brachytherapy, a fixation device may be used to minimize applicator motion from the simulation to the end of treatment.

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 IV or oral contrast agents and the handling of tissue densities when contrast is used.

EBRT

Photon/Proton Therapy

Prior to simulation, wires or other radio-opaque markers may be used on gross disease. Vaginal markers which distend the vagina are not generally recommended. Moderate bladder filling is encouraged for simulation and treatment.

A CT simulation scan is required with a slice thickness ≤ 3.0 mm. The scan should extend from L1 to mid-thigh or from carina to mid-thigh (when paraaortic lymph nodes are involved). One scan is obtained with the bladder full and one with the bladder empty. These scans will be fused to contour the internal target volume (ITV). IV contrast and bowel prep-contrast are allowed for better delineation of the pelvic vessels and small bowel. 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

Prior to simulation, it is advised that a Foley catheter be inserted into the bladder at the outset of the procedure. Fiducial markers can be implanted in the target volume to assess applicator or catheter displacement.

All subjects will undergo a CT or MR simulation scan or MR cross-sectional imaging with a slice thickness ≤ 3.0 mm with contrast. The images should contain the entire brachytherapy applicators and critical structures including the bladder and rectum. For MRI, T2 weighted images are to be used for planning. T1 MRI images may be used for co-registration of applicator as the titanium artifact may be less on this sequence.

Motion Management Technique

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

EBRT

The motion due to bladder filling can be taken into consideration in defining the ITV. Patients are simulated with a full and empty bladder to evaluate 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. 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

In HDR brachytherapy, a fixation device can minimize applicator motion. Periodic checks during PDR/LDR brachytherapy, and initial and final checks in HDR brachytherapy are recommended to monitor changes in the applicator position.

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

A 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 most cases, the diagnostic MRI to CT simulation fusion should focus on the area of interest i.e., the primary tumor and not on pelvic bone. For MR-guided treatment, the diagnostic studies should be fused to the planning MRI.

Brachytherapy

For volume-directed brachytherapy, pelvic MRI is suggested at least with either the first or second insertion. Subsequent insertions may use CT or MRI for planning. Ideally MRI-based brachytherapy would involve MRI only simulations for each treatment fraction to minimize uncertainties associated with applicator and organ motion during transferring patient between imaging modalities as well as uncertainties related to image registration (AAPM TG 303 report). Deformable image registration between MRI and CT simulation scans is not encouraged to avoid deforming the tumor.

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 quality assurance (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)
PTV_dose-xx	PTV receiving cGy minus xx mm from skin surface	Required when applicable (Photon only)

Detailed Specifications

Target volumes: The definitions of volumes will be in accordance with the 1999 ICRU Report 62.

GTV_: The GTV is defined as all gross disease and involved lymph nodes determined from the radiographic studies, clinical information, physical examination, and/or biopsy results.

CTV_: The CTV includes the gross tumor, the entire cervix, and uterus, parametria, part or all of the vagina as well as external, internal, common iliac, presacral lymph nodal regions or paraaortic lymph nodal regions.

ITV_: If appropriate for the study, patients can be simulated with both a full and empty bladder (i.e., 2 simulation scans). The gross tumor, the entire cervix and uterus are contoured in both scans and the two scans are fused to generate ITV. If on-board adaptive RT is to be utilized, then the use of a bladder ITV may not be necessary, but one should still account for intra-fraction bladder motion in their margin strategy.

PTV_: The PTV is defined as the CTV or the ITV plus an appropriate margin. 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.

Brachytherapy Point-directed

Standard name	Description	Validation Required/Required when applicable/Optional
Point_A	ICRU 38 point description	Required

Volume-directed

Ideally MRI based target delineation should be performed to identify the GTV at each treatment fraction of brachytherapy. If MRI access is limited, the MRI for the first treatment fraction can be reused by superimposition in the process of contouring on CT for subsequent fractions. No planning margins will be added to CTV_HR.

Standard name	Description	Validation Required/Required when applicable/Optional
GTV	GTV to receive Gy	Required if visible at the time of brachytherapy
CTV_HR	CTV_HR to receive Gy	Required
CTV_IR	CTV_IR to receive Gy	Study dependent

Detailed Specifications

Target volumes: The definitions of target volumes will be in accordance with the 2013 ICRU Report 89 and GEC-ESTRO/ABS recommendations.

GTV: Macroscopic tumor (if present) at time of brachytherapy

High Risk CTV (CTV_HR): GTV + whole cervix + extra cervical tumor extension at time of brachytherapy

Intermediate Risk CTV (CTV_IR): CTV_HR + 5 - 15 mm margin at time of brachytherapy

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 when applicable
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.

Brachytherapy

Point-directed

Standard name	Description	Validation Required/Required when applicable/Optional
Point_Rectum	Rectum ICRU 38 point description	Required
Point_Bladder	Bladder ICRU 38 point description	Required
Point_VaginalSurf	Vaginal Surface ICRU 38 point description	Required when applicable

Volume-directed

Standard name	Description	Validation Required/Required when applicable/Optional
Rectum	Rectum	Required
Bladder	Bladder	Required
Sigmoid	Sigmoid	Required
Bowel	Bowel Loops	Required when applicable

Detailed Specifications

Rectum: Rectum is contoured as a whole for volume-directed brachytherapy

Bladder: Bladder is contoured as a whole for volume-directed brachytherapy

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

Pelvis/Pelvis +SIB

Target standard name	Dose (Gy)	Fraction size (Gy)	# of fractions	Frequency	Dose specification technique
PTV_4500	45	1.8	25	Daily	Covering 95% of PTV
PTV_5000	50	2.0	25	Daily	Covering 95% of PTV
PTV_5040	50.4	1.8	28	Daily	Covering 95% of PTV
PTV_ (SIB only)	50.4-59.4	>2.0	25-28	Daily	Covering 95% of PTV

Parametrial and/or Nodal Boost (Sequential)

A parametrial or nodal boost of 5.4 - 14.4 Gy at 1.8 Gy/fraction may be delivered. Volume-based prescription is possible for 3D-CRT.

Target standard name	Dose (Gy)	Fraction size (Gy)	# of fractions	Frequency	Dose specification technique
PTV_	5.4-14.4	1.8	3-8	Daily	Prescription dose to isocenter or 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

HDR Point A directed implant

Total EBRT (Gy)	# of HDR fractions	HDR Point A dose/fraction (Gy)	Total HDR Point A dose (Gy)	Total Point A EQD2Gy(10) (Gy)
45	4	7.0	28.0	83.9
45	5	5.5	27.5	79.8
45	5	6.0	30.0	84.3
50	4	7.0	28.0	89.7
50	5	5.5	27.5	85.5
50	5	6.0	30.0	90.0
50.4	4	7.0	28.0	89.2
50.4	5	5.5	27.5	85.1
50.4	5	6.0	30.0	89.6

where EQD2Gy = Total Biological Equivalent Dose in 2 Gy Fractions

HDR Volume-directed implant

The HDR brachytherapy dose (27.5-30 Gy) can be prescribed to CTV_{HR} but point A dose must be documented.

PDR/LDR Point A directed implant

Total EBRT (Gy)	# of PDR/LDR fractions	Point A dose/fraction (Gy)	Total PDR/LDR Point A dose (Gy)	Total Point A dose (Gy)
45	1	35-40	35-40	80-85
45	2	17.5-20	35-40	80-85
50	1	35-40	35-40	85-90
50	2	17.5-20	35-40	85-90
50.4	1	35-40	35-40	85.4-90.4
50.4	2	17.5-20	35-40	85.4-90.4

PDR Volume-directed implant

The PDR brachytherapy dose (35-40 Gy) can be prescribed to CTV_{HR}.

In general, HDR insertions should start during the fourth or fifth week of EBRT and be separated by a minimum of 48 hours, and no more than 3 insertions should be performed per week. Iridium-192 is the preferred source for HDR brachytherapy. In LDR brachytherapy, if 2 insertions are used, they should be separated by a minimum of 5 - 7 days and maximum of 21 days. If 2 insertions are used, the second implant should be completed within three weeks of the completion of EBRT. Cesium-137 is the preferred source for LDR brachytherapy. PDR brachytherapy can be delivered using an Iridium-192 source with the same schedule as LDR. EBRT and brachytherapy may not be administered on the same day. All brachytherapy sources must be listed on the joint AAPM/IROC Houston Registry of Brachytherapy Sources to be utilized on NCTN clinical trials

(http://irochouston.mdanderson.org/RPC/BrachySeeds/Source_Registry.htm).

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 the 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

Pelvis/Pelvis +SIB

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

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

Parametrial and/or Nodal Boost (Sequential)

Name of structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Notes (Please remove this column when notes are
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				not needed)
PTV	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.

EBRT Photon + HDR/PDR Volume-directed Brachytherapy

Dose contribution from EBRT is assumed to be prescription dose and cumulative doses to GTV and CTV are EQD2Gy(10) ($\alpha/\beta=10$ for early effects) for HDR and physical doses for PDR. However, deformable image/dose registration between EBRT CT and brachytherapy CT can be performed to calculate cumulative doses to GTV and CTV.

Name of structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Notes (Please remove this column when notes are not needed)
CTV_HR	D90% [Gy]	>=85	-	
	D98% [Gy]	>=75	-	
CTV_IR	D98% [Gy]	>=60	-	

Per Protocol range is excluded from Variation Acceptable range.

Normal Structure Constraints and Compliance Criteria

EBRT

Photon Therapy (Pelvis (IMRT) + Parametrial and/or Nodal Boost (SIB or Sequential))

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	D50% [Gy]	<=45	<=54	
	D0.03cc [Gy]	<=50	<=55	

Bladder	D50% [Gy]	<=45	<=55	
	D0.03cc [Gy]	<=50	<=57.5	
Spc_Bowel	D30% [Gy]	<=40	<=50	
	D0.03cc [Gy]	<=59.4	<=62.1	
Bowel Loop* (On-board adaptive)	D30% [Gy]	<=40	<=50	
	D0.03cc [Gy]	<=59.4	<=62.1	
Femurs	D15% [Gy]	<=30	<=50	
	D0.03cc [Gy]	<=50	<=55	
BoneMarrow (if applicable)	Mean [Gy]	<=27	<=29	
	V10Gy [%]	<=85.5	<=90	
	V20Gy [%]	<=66	<=75	

Per Protocol range is excluded from Variation Acceptable range.

*When on-board RT is being used the bowel loops should be contoured instead of the SPC_Bowel approach.

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).

EBRT Photon + Brachytherapy

Dose contribution from EBRT is assumed to be prescription dose and the following dose criteria is EQD2Gy(3) ($\alpha/\beta=3$ for late effects) for HDR and physical dose for PDR/LDR.

Name of structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Notes (Please remove this column when notes are not needed)
HDR Point-directed				
Point_Rectum	Dpoint [Gy]	<=75	<=80	
Point_Bladder	Dpoint [Gy]	<=80	<=85	
Point_VaginalSurf	Dpoint [Gy]	<=150	<=175	
HDR/PDR Volume-directed				
Rectum	D2cc [Gy]	<=65	<=75	
Bladder	D2cc [Gy]	<=80	<=90	
Sigmoid	D2cc [Gy]	<=70	<=75	
PDR/LDR Point-directed				
Point_Rectum	Dpoint [Gy]	<=80	<=85	
Point_Bladder	Dpoint [Gy]	<=85	<=90	
Point_VaginalSurf	Dpoint [Gy]	<=150	<=175	

Per Protocol range is excluded from Variation Acceptable range.

For volume-directed brachytherapy, uniform dose volume reporting according to the ICRU Report 89 and GEC-ESTRO recommendations. For each fraction the following parameters should be recorded:

- TRAK
- D100 and D98 for GTV, CTV_HR and CTV_IR
- D90 for GTV and CTV_HR
- D50 for CTV_HR
- V100 for CTV_HR
- D2cc of the bladder, rectum, sigmoid and small bowel (for HDR, EQD2Gy(3) (Gy) per formula $EQD2Gy = D * [(d + \alpha/\beta)/(2 + \alpha/\beta)]$ using $\alpha/\beta=3$).

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.)			
Overall Treatment time	≤ 56 days	≤ 67 days	

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. Bowel
3. Rectum
4. Bladder
5. Femurs
6. Bone Marrow (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.

Brachytherapy

1. CTV (if volume-directed plan used)
2. Sigmoid
3. Rectum
4. Bladder

If dose constraints of critical structures are exceeded, the following solution is suggested:

For volume-directed brachytherapy, if the treatment planning system provides a manual optimization option, the plan can be manually optimized to reduce dose to the critical structures as long as D90 of CTV meets target volume constraints. The use of interstitial brachytherapy is sometimes useful to improve the coverage and decrease the OAR dose but this technique should be used when indicated

and by trained physicians.

- 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, except for when MRI-Linac is being used for treatment. 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 CT images are the primary dataset for dose calculation. If MR images are used for dose calculation, a method of correcting image distortion and tissue density should be applied.

Heterogeneity corrections are not mandatory.

- Dose matrix resolution

Dose grid size should be ≤ 3.0 mm (preferably ≤ 2.0 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 1.0 mm 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.

Brachytherapy

To monitor changes in the position of the applicators, periodic checks during LDR brachytherapy and initial and final checks in HDR brachytherapy are necessary. A fixation device and/or angulometers attached to the applicators can provide information on cephalocaudal position displacement and/or sagittal and coronal rotations. Ideally, the treatment setup would be verified using 3D imaging such as CT or kV CBCT to assess applicator to fiducial markers consistency.

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 QA Review after EBRT and brachytherapy cases enrolled have been received at IROC Philadelphia and IROC Houston respectively.