NRG ONCOLOGY PROTOCOL DEVELOPMENT TEMPLATE FOR RADIATION THERAPY

DISEASE SITE: Whole Breast
SUB-COMPONENT: Photon and Proton Therapy

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Underlined highlighted texts are either instructions or suggestions to be deleted or replaced by PIs with regular texts without highlight.

Regular highlighted texts are examples to be selected (remove highlight), deleted or replaced by PIs with regular texts**.**

In this section, the modality used to deliver radiation, the method for patient immobilization, and the method to correlate patient geometry and delivery geometry should be clearly described. Requirements for credentialing (including the phantom irradiation credentialing and the IGRT credentialing) should be explicitly specified in the protocol.

[STUDY CHAIRS: Refer to the NRG web site for RTQA Protocol Prescription Guidelines for writing RT prescriptions in NRG protocols [*link to come*].]

Radiation Therapy Schema

Schema at the beginning of the protocol should be followed.

Proton dose shall be reported in cGy (RBE) where the physical proton dose is multiplied by a uniform RBE value equal to 1.1. Proton and photon doses are considered equivalent in terms of biological response for this protocol.

5.2.1 Treatment Technology

List allowed Treatment Modalities (including energy): photons, protons, electron, brachytherapy, ….. Required Capabilities: IMRT, IGRT, gating, etc.

Radiation therapy may be delivered in whole or in part using the following beam modalities and delivery techniques:

- Externally administered megavoltage photon beams, via either forward-planned 3DCRT, inverse-planned 3DCRT, or inverse-planned IMRT, VMAT, tomotherapy (e.g. helical tomotherapy, Accuray TomoTherapy or Radixact), or topotherapy (e.g. "TomoDirect," Accuray TomoTherapy or Radixact).
- Externally administered proton beams, via either 3D conformal proton therapy (3DCPT) using passive scattering technique or uniform scanning, or intensity modulated proton therapy (IMPT) technique using scanning pencil beams.
- Externally administered megavoltage electron beams (for primary IMC or post-lumpectomy boost irradiation)
- Interstitial brachytherapy techniques (for post-lumpectomy boost irradiation)

5.2.2 Immobilization and Simulation

Immobilization

Proper immobilization is critical for this protocol. Patient setup reproducibility must be achieved using appropriate clinical devices.

During simulation imaging, the patient may be positioned supine, prone, or in a lateral decubitus position as appropriate for patient comfort, sparing of OARs, or access to the target volumes:

- For supine positioning, the ipsilateral arm shall be positioned superior to the patient for photon therapy. For proton therapy, arm down position is allowed when patient has difficulty raising arms above head; the contralateral arm may be positioned superiorly as well. A wedge may be placed beneath the patient's back. Reproducible breath holds or free breathing may be used for setup. If a breath-hold CT acquisition (e.g. deep inspiration breath hold, DIBH) is performed, a method to ensure reproducibility of the respiratory phase at which the breath is held as well as the patient geometry during breath hold is required. Methods include external or internal fiducial tracking, spirometry, fluoroscopy and surface-guided imaging.
- For prone positioning, the ipsilateral arm shall be positioned superior to the patient; the contralateral arm should be positioned superiorly as well. An aperture to accommodate the ipsilateral breast, to allow it to hang downward, shall be incorporated into the platform upon which the patient rests. The platform shall also displace the contralateral breast laterally and posteriorly away from the ipsilateral breast. The attenuation of beams through the immobilization hardware (e.g. contralateral prone breast board) shall be properly accounted for in the treatment planning system (TPS).
- For lateral decubitus positioning, the ipsilateral arm shall be positioned superior to the patient so as to facilitate access of the treatment beams to the target volume. If lateral decubitus positioning is used for to deliver a separate boost irradiation, the protocol shall be consulted regarding requirements for accurate assessment of cumulative dose, such as the use of deformable image registration and image fusion.

The patient's thoracic region and cranially-extended arms shall be immobilized using either a breast board, vacuum-bag (i.e. VacLoc) or molded foam (i.e. Alpha Cradle) techniques. Novel immobilization hardware may be used, provided that it conforms to the requirements of the protocol and is approved by the protocol study reviewers.

Motion Management Technique

Please remove this subsection when motion management is not used.

Motion management should be considered for this protocol. The types of motion management allowed on this study are four-dimensional computed tomography (4DCT), active breath-hold, deep inspiration breath hold (DIBH), active breathing control (ABC), and gating.

Respiratory-correlated images may be acquired during simulation to facilitate phase-specific gated radiation therapy or breath-hold radiation therapy, subject to the requirements and restrictions of the protocol. If a 4D simulation is performed, the respiratory phase-specific image (e.g. end-inhalation, end-exhalation, or intermediate phase) or specific 4D projection image (e.g. average intensity projection, maximum intensity projection) to be used as the primary planning image and/or for target-volume definition purposes shall be indicated. If a breath hold simulation is performed, reproducibility of the breath hold image acquisition and consistency of the breath hold position between simulation and treatment shall be established.

Target Localization for Simulation

Depending upon the requirements of the protocol, radio-opaque wires shall be placed upon the surface of the superior, inferior, lateral, or medial extents of the ipsilateral breast, and directly on the surgical scar left from a lumpectomy or mastectomy, if applicable, to clearly delineate the scar's location. The borders of the ipsilateral breast or chest wall are defined in Table 2 of Section 5.2.4. During simulation, localizing permanent (e.g. tattoos), temporary or semi-permanent marks (e.g. tape, marker) shall be placed on the skin surface to denote a setup reference point for planning and pre-treatment positioning. A reproducible method should be used to enable identification of the setup reference point within the TPS. If decubitus positioning is used, marks shall not be obstructed by the couch or the immobilization hardware. Radio-opaque fiducials on the skin surface shall be corrected during the treatment planning process in a manner documented in Section 5.2.3. In situations where an institution has a robust surface-guided imaging program for simulation and daily localization, the institution can follow their practice, including if patients do not receive tattoos.

At the discretion of the protocol, tissue expanders may be present for post-mastectomy chest wall cases during the planning simulation and for each EBRT fraction, provided that the geometry of the expansion is repeatable between each fraction. Note that since accurate CT-number determination may not be possible for tissue expanders due to the image artifacts they may produce, it is necessary to contour the expanders during the planning process, override the density using the known composition of the expander, and also correct for image artifacts within the regions proximal to the expanders. A conventional tangent-field technique encompassing the expanded chest wall is acceptable. Lower-energy photons are recommended, since dose hot spots proximal to the expanders can arise due to increased pair production from the interaction of 15MV and 18MV photons interacting with high-atomic-number materials.

For proton therapy, the filling of the expander should remain consistent from the CT simulation to the end of treatment course. The expander shall be full or near full to best optimize the dose distribution and the setup reproducibility.

Bolus:

For instances in which enhancement of prescribed dose to the skin surface is deemed necessary, such as for post-surgical scars to the breast or post-mastectomy chest wall, or to the post-mastectomy chest wall if it is suspicious for disease, skin bolus may be used. Acceptable bolus compositions include materials which can be conformed to the patient's surface such as tissue-equivalent Superflab, Aquaplast, molded wax, or other customized materials such as 3D printing (in house or commercially available such as .decimal), and brass mesh bolus etc. An acceptable range of bolus thickness is 0.3 cm to 1 cm. If the bolus is not explicitly imaged during acquisition of the planning image, its geometry and composition must be accurately defined within the TPS. Detailed instructions to ensure consistent placement of the bolus prior to each fraction shall be provided and documented. Note that during the treatment course the bolus placement may be prescribed daily or at some other frequency (e.g. every other day). At the attending physician's discretion, the use of bolus may be discontinued due to factors including the appearance of unexpected skin reactions.

5.2.3 Simulation Imaging

Please indicate "Not applicable" if it does not apply to your protocol. Please do not delete this subsection.

This subsection should include information about the extent of CT and MR imaging, the resolution of the scan information including the slice thickness, and details of the allowed use of contrast agents and the handling of tissue densities when contrast is used.

CT-based simulation imaging

Depending upon the requirements and restrictions of the protocol, the primary volumetric image acquired for target delineation and dose calculation purposes may be a CT image. The Field of View (FOV) and superior-inferior extent of the primary planning image shall be large enough to encompass the target volume, the entirety of OARs in close proximity to the target, and any regions through which treatment beams may enter or exit through the patient.

The reconstructed axial slice thickness shall, in the vicinity of the target volumes, be sufficient to enable accurate dose calculation resolution. The protocol recommends a reconstructed slice thickness of 0.3 cm or less in this region. For regions of the patient either superior or inferior to the target-volume region, a greater slice thickness may be used (up to 0.5 cm), with the scan range extending superiorly and inferiorly from the boundaries of the target volume (5 cm in each direction) to accurately calculate lateral scatter within the TPS.

MR-based simulation imaging

Although the primary data set for the basis of radiotherapy dose calculations shall be from a CT acquisition, MR images may also be acquired for the purposes of target delineation. The FOV and superior-inferior extent of the primary planning image shall be large enough to encompass the target volume, the entirety of the OARs, and any regions through which treatment beams may propagate through the patient. MRI images or synthetic CTs (from other modalities) should not be used as the primary planning images for proton therapy.

The reconstructed axial slice thickness shall, in the vicinity of the target volumes, be sufficient to enable accurate dose calculation resolution. The protocol recommends a reconstructed slice thickness of 0.3 cm or less in this region. For regions of the patient either superior or inferior to the target-volume region, a greater slice thickness may be used (up to 0.5 cm), with the scan range extending superiorly and inferiorly from the boundaries of the target volume (5 cm in each direction) to enable accurate calculation of lateral scatter within the TPS.

Multimodality simulation imaging

Additional images may be acquired to refine the definition of the target volumes; these include contrast-enhanced CT images (for example, to visualize the LADA), functional MR images, and nuclear medicine images (e.g. PET, SPECT). Depending upon the anatomic region being treated, either rigid registration or deformable registration may be used. It is expected that the registration will be based to the appropriate region(s) as appropriate. The local accuracy of the target registration and the retention of the breast shape shall be verified.

Artifacts in the Planning Image

If the following categories of artifacts are present in the planning image, they may be resolved using the following techniques:

- *Insufficient field of view*: the patient may be positioned such that the ipsilateral breast and proximal skin surfaces are fully encompassed within the FOV. However, the entirety of the OARs tabulated in Section 5.2.5 must also be fully included in the FOV; no extrapolation of the OAR contours outside the FOV is permitted. For all planning techniques, treatment beam trajectories entering through regions truncated by the image FOV are not permitted.
- *Motion artifacts*: if there are residual motion artifacts that can be accounted for without re-simulation, available data from imaging techniques such as 4DCT should be evaluated to determine if an appropriate volume can be defined. Whichever technique is used shall result in a planning image to best represent the geometry expected to be present during EBRT. Prone positioning may be used in place of supine positioning to minimize motion in the vicinity of the ipsilateral breast.
- *Image density artifacts*: if low-density or high-density "streaks" or beam-hardening artifacts appear in the image within regions known to be of uniform density, density-override contours may be drawn to encompass these artifacts, with an appropriate density forced within these contours. Residual contrast agent apparent within the planning image (an example being iodine contrast infused during CT simulation to visualize the LADA) should be similarly contoured, with the appropriate density override within the contour. Note that radio-opaque fiducials present on the skin surface during the planning CT simulation shall be corrected in this manner as well, if they cannot otherwise be excluded from the patient external contour and the subsequent dose calculation within the TPS. These considerations apply to photon and proton planning.

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

<u>Please remove this subsection if it does not apply to your protocol.</u>

Functional imaging techniques such as FDG-PET/CT imaging may be used as part of staging and to assist in volume delineation in all eligible patients.

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.

Delineation may be done either manually, or through an auto-segmentation process (using either image grayscale level differences or anatomic site-specific atlases), provided that all contours are verified manually.

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 shall include crucial items such as boundary definitions and margins.

Depending upon which disease sites are to be treated for the protocol, for each of the treated volumes the contour labels, description of the target, delineation guidelines, and validation requirements are tabulated below. Note that these target volumes are adapted from RTOG 1005 and NSABP B-51/RTOG 1304. Each of the target volume labels shall be appended with "_R" or "_L" to indicate whether the treated volume is right-sided or left-sided, respectively. The standard names of the targets and OARs are following the guideline of AAPM TG 263. Validation may either be Required, Required when applicable, or Optional:

Table 1: Delineation and validation guidelines for target volumes (see the special considerations regarding proton therapy PTV expansion)

Standard Name	Description	Delineation guidelines	Validation **Required/Required when applicable/Optional**
GTVsb	gross tumor volume (GTV) for surgical bed (Lumpectomy)	contour the lumpectomy bed as apparent on planning image, including the excision cavity volume, architectural distortion, lumpectomy scar, seroma, and surgical clips when present	**Required**
CTVsb	Surgical bed (lumpectomy cavity) CTV; clinical target volume (CTV) including regions of the GTV suspicious for subclinical disease	include the GTVsb plus 1.0 to 1.5 cm of surrounding breast tissue, but exclude the pectoralis muscle, all chest wall muscles, ribs, and	**Required**

		regions exterior to the patient surface	
PTVsb	Surgical bed (lumpectomy) PTV	CTVsb + 0.5 cm (if IGRT used) or 1.0 cm (if no IGRT) expansion in all directions; exclude heart	**Required**
PTVsb_Eval	PTV evaluation volume; PTV minus overlapping critical structure ROIs; relevant regarding boosts to the lumpectomy site	retract PTVsb by 0.5 cm distal to the skin surface, to avoid skin reactions from boost fields; do not extend beyond breast tissue, and do not cross midline (consistent with RTOG 1005)	**Required**
CTV_Breast	whole breast CTV; ipsilateral (to be treated) breast	include the glandular breast tissue as apparent on the planning image, incorporating the anatomic borders as summarized in Table 2, and include the lumpectomy CTV	**Required**
PTV_Breast	whole breast PTV; ipsilateral (to be treated) breast	whole breast CTV + 0.5 cm (if IGRT used) or 1.0 cm (if no IGRT) 3D expansion; exclude heart, rib; do not cross midline	**Required**
PTV_Breast_Eval	whole breast PTV evaluation volume; ipsilateral (to be treated) breast	recede PTV_Breast by 0.5 cm distal to the skin surface, to avoid skin	**Required**

		reactions from boost fields	
GTV_Scar	mastectomy or lumpectomy scar GTV	radio-opaque wire placed atop scar during simulation, and including visible postoperative changes distal to the wire	**Required when applicable**
CTV_Scar	mastectomy or lumpectomy scar CTV	scar + 1.0 cm 3D expansion; exclude ribs; do not cross midline	**Required when applicable**
PTV_Scar	mastectomy or lumpectomy scar PTV	scar CTV + 0.5 cm (if IGRT used) or 1.0 cm (if no IGRT) expansion; exclude heart	**Required when applicable**
PTV_Scar_Eval	mastectomy or lumpectomy scar PTV evaluation volume	recede PTV_Scar by 0.5 cm distal to the skin surface, to avoid skin reactions from boost fields	**Required when applicable**
CTV_CW	chest wall CTV; ipsilateral (to be treated) chest wall	should incorporate the anatomic borders described in Table 2 and include the mastectomy scar	**Required when applicable**
PTV_CW	chest wall PTV; ipsilateral (to be treated) chest wall	chest wall CTV + 0.5 cm (if IGRT used) or 1.0 cm (if no IGRT) expansion; exclude heart; do not cross midline	**Required when applicable**
PTV_CW_Eval	chest wall PTV evaluation volume	recede PTV_CW by 0.5 cm distal to the skin surface, to avoid skin	**Required when applicable**

		reactions from boost fields	
CTVn_Sclav	supraclavicular CTV; includes the ipsilateral supraclavicular nodal group	depends on the specific clinical case and should take into account the anatomic borders described in Table 2	**Required when applicable**
PTVn_Sclav	supraclavicular PTV; includes the ipsilateral supraclavicular nodal group	supraclavicular CTV + 0.5 cm expansion; exclude thyroid, trachea, esophagus, lung, vertebral body, and skin minus 0.5 cm	**Required when applicable**
CTVn_Ax	axillary nodal CTV; includes the ipsilateral axillary nodal group	depends on the specific clinical case and should take into account the anatomic borders described in Table 2; the three levels of the axilla may overlap caudal to cranial	**Required when applicable**
PTVn_Ax	axillary nodal PTV; includes the ipsilateral axillary nodal group	axillary CTV + 0.5 cm; exclude lung	**Required when applicable**
CTVn_IMN	internal mammary nodal CTV; includes the ipsilateral internal mammary chain of nodes	depends on the specific clinical case and should take into account the anatomic borders described in Table 2	**Required when applicable**
PTVn_IMN	internal mammary nodal PTV; includes the ipsilateral	IMN CTV + 0.5 cm medially, laterally, superiorly, and	**Required when applicable**

	internal mammary chain of nodes	inferiorly; exclude heart, lung, breast, and chest wall	

Detailed Specifications

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

Special considerations are needed for proton treatments. In this situation the margin is determined from the CTV based on beam arrangement to account for lateral setup uncertainty as well as proton range uncertainty along the beam direction. As a consequence, a beam-specific PTV (BsPTV) for each beam orientation is needed. This would be practically unworkable to record or report the dose distribution to 'PTV if there were a separate BsPTV for each beam. ICRU 78 recommends that the PTV be defined relative to the CTV on the basis of lateral uncertainties alone and that an adjustment is made within the beam-design algorithm to take into account the uncertainties along the beam direction. Therefore, for each beam, a 5 mm lateral (relative to the beam directions) margin will be added. The PTV is defined as the union of the BsPTVs and may not extend beyond bony margins or the skin surface. This PTV will be used to report dose, per ICRU 78. An adjustment must be made within the beam-design algorithm to take into account the range uncertainties along the beam direction.

Accounting for Tumor Motion Approaches:

Internal margin (IM):
The IM used will be dictated by the motion management decision made at time of simulation.
1. If the simulation is done with a free-breathing CT only (not correlated with respiratory motion or otherwise compensating for such motion), the IM will be 1.0 cm in the superior-inferior direction and 0.5 cm in the axial direction.
2. If simulation is done using an active breath-hold, deep inspiration breath hold, or gated breathing technique, the IM will be 0.5 cm in all directions.
3. If simulation is done using a 4DCT to develop a maximum intensity projection of the tumor volume, no IM is needed.

Setup margin (SM):
Daily IGRT is a requirement for this trial with proton therapy; therefore, the SM will be 0.5 cm in all directions.

The anatomic boundaries of the breast and chest wall contours, along each of the superior-inferior, anterior-posterior, and lateral-medial directions, are tabulated below:

Table 2: Delineation guidelines for the breast and chest wall

Target volume label	Superior	Inferior	Anterior	Posterior	Lateral	Medial

Breast_L (left sided treatment) or Breast_R (right sided treatment)	clinical reference + second rib insertion	clinical reference + loss of image-apparent breast	skin	excludes pectoralis muscles, chest wall muscles, ribs	clinical reference + midaxillary line (typically), excludes latissimus (lat.) dorsi muscle	sternum-rib junction
Chestwall_L or Chestall_R	inferior border of the clavicular head	clinical reference + loss of image-apparent contralateral breast	same as above	rib-pleural interface (anterior surface of pectoralis muscles, chest wall muscles); excludes ribs	Clinical reference/midaxillary line (typically), excludes latissimus dorsi muscle	sternum-rib junction

Notes:

(a) following lumpectomy for breast-only treatment

(b) superior border is highly variable, depending upon breast size and patient position; the lateral aspect can be more cephalad than the medial aspect, depending upon breast shape and patient position

(c) lateral border is highly variable depending upon breast size and amount of ptosis

(d) medial border is highly variable depending on breast size and amount of ptosis; clinical reference needs to be taken into account; should not cross midline

(e) CTV after lumpectomy for more locally advanced cases; this includes those with clinical stages IIb and III who receive neoadjuvant chemotherapy and lumpectomy and who have sufficient disease risk to require post-mastectomy radiation, had a mastectomy been done

(f) CTV after mastectomy

(g) lateral border meant to estimate the lateral border of the previous breast; typically extends beyond the lateral edge of the pectoralis muscles but excludes the latissimus dorsi muscle; the lateral extent of mastectomy scar should be encompassed

(h) clinical reference marks need to be taken into account; the chest wall typically should not cross midline; the medial extent of mastectomy scar should typically be included

The anatomic boundaries of each of the regional nodal groups, along with each of the superior-inferior, anterior-posterior, and lateral-medial directions, are tabulated below.

Table 3: Delineation guidelines for regional lymph nodes

Target volume label	Superior	Inferior	Anterior	Posterior	Lateral	Medial
LN_Sclav_L or LN_Sclav_R (ipsilateral side)	inferior to the cricoid cartilage	junction of brachioceph.–axillary vns./ caudal edge clavicle head (a)	as apparent on planning image	anterior aspect of the scalene muscles	superior: lateral edge of SCM muscle; inferior: junction first rib–clavicle	excludes the thyroid and trachea
LN_Ax_L1_L or LN_Ax_L1_R (ipsilateral side)	where axillary vessels cross lateral edge of pectoralis minor	where pectoralis major inserts into ribs (b)	plane defined by anterior surface of pectoralis major and latissimus dorsi	anterior surface of subscapularis	medial border of latissimus dorsi	Lateral border of pectoralis minor
LN_Ax_L2_L or LN_Ax_L2_R (ipsilateral side)	where axillary vessels cross medial edge of pectoralis minor	where axillary vessels cross lateral edge of pectoralis minor (c)	anterior surface of pectoralis minor	ribs and intercostal muscles	lateral border of pectoralis minor	medial border of pectoralis minor
LN_Ax_L3_L or LN_Ax_L3_R (ipsilateral side)	where pectoralis minor inserts on cricoids	where axillary vessels cross medial edge of pectoralis minor (d)	posterior surface of pectoralis major	ribs and intercostal muscles	medial border of pectoralis minor	ribs
LN_IMN_L or LN_IMN_R	superior aspect of the medial first rib	superior aspect of the fourth rib	see note (e) below	see note (e) below	see note (e) below	see note (e) below

(ipsilateral side)						

Notes:

(a) supraclavicular caudal border meant to approximate the superior aspect of the breast/chest wall field border

(b) axillary level I caudal border is clinically at the base of the anterior axillary line

(c) axillary level II caudal border is the same as the cephalad border of level I

(d) axillary level III caudal border is the same as the cephalad border of level II

(e) internal mammary lymph nodes encompass the internal mammary/thoracic vessels

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 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, third columns. The detailed specifications have to include crucial items such as boundary definitions and margins.

For each of the critical structures the contour label, description of the target, delineation guidelines, and validation requirements are tabulated below. Note that these target volumes are adapted from NSABP B-51/RTOG 1304. Each of the target volume labels should be appended with "_R" or "_L" to indicate whether the treated volume is right-sided or left-sided, respectively. The standard names of the targets and OARs are following the guideline of AAPM TG 263. Validation may either be Required, Required when applicable, or Optional:

Table 4: Validation guidelines for organs at risk

Standard Name	Description	Validation **Required/Required when applicable/Optional**
Lung_R	right lung	**Required**
Lung_L	left lung	**Required**
Heart	heart	**Required**

Thyroid	thyroid	**Required**
Breast_L	left breast	**Required**
Breast_R	right breast	**Required**
SpinalCord	spinal cord	**Required**
BrachialPlex_R	right brachial plexus	**Required**
BrachialPlex_L	left brachial plexus	**Required**
External	patient skin surface	**Required**

Detailed Specifications

The anatomic boundaries of the heart and lung, along each of the superior-inferior, anterior-posterior, and lateral-medial directions, are tabulated below:

Table 5: Delineation guidelines for organs at risk

Organ at risk	Superior	Inferior	Anterior	Posterior	Lateral	Medial
Breast_R (left sided treatment) or Breast_L (right sided treatment)	clinical reference + second rib insertion	clinical reference + loss of image-apparent breast	skin	excludes pectoralis muscles, chest wall muscles, ribs	clinical reference + midaxillary line (typically), excludes latissimus (lat.) dorsi muscle (b)	sternum-rib junction
Heart	the heart should be contoured beginning just inferior to the level in which the pulmonary trunk branches into the left and right pulmonary arteries (PA)	location where the heart is no longer apparent on the planning image; the heart blends with the diaphragm and the liver at its inferior aspect; adjusting	pericardium	excludes descending aorta, esophagus, and vertebral body	pericardium	pericardium

		the window and level settings can assist in discerning the heart from these adjacent organs				
Lung_L or Lung_R (ipsilateral side)	pleura	pleura	pleura	pleura	pleura	pleura
Thyroid	all "bright: thyroid tissue	all "bright: thyroid tissue	all "bright: thyroid tissue	all "bright: thyroid tissue	all "bright: thyroid tissue	all "bright: thyroid tissue
SpinalCord	foramen magnum (or superior-most planning image slice, if foramen magnum not included)	inferior aspect of L3 vertebra (or inferio-most planning image slice, if L3 not included)	as apparent on the planning image	as apparent on the planning image	as apparent on the planning image	as apparent on the planning image
BrachialPlex_R (for right-sided treatment) or BrachialPlex_L (for left-sided treatment)	guidelines provided by reference (g)	guidelines provided by reference (g)	guidelines provided by reference (g)	guidelines provided by reference (g)	guidelines provided by reference (g)	guidelines provided by reference (g)

Notes:

(a) superior border is highly variable, depending upon breast size and patient position; the lateral aspect can be more cephalad than the medial aspect, depending upon breast shape and patient position
(b) lateral border is highly variable, depending upon breast size and amount of ptosis
(c) medial border is highly variable, depending on breast size and amount of ptosis; clinical reference needs to be taken into account; should not cross midline
(d) the following structures, if identifiable, should be excluded from the heart contour: esophagus, great vessels (ascending and descending aorta, inferior vena cava); one need not include pericardial fat, if present; contouring along the pericardium itself, when visible, is appropriate
(e) the lung volume within the pleural surface, excluding the ribs, mediastinum, and

diaphragm, can be auto-contoured (using grayscale-level differences) by most planning systems; the contours shall be verified manually

(f) the thyroid is easily visible on a non-contrast CT due to its preferential absorption of iodine, rendering it "brighter" or denser than the surrounding neck soft tissues; the left and right lobes of the thyroid are somewhat triangular in shape and often do not converge anteriorly at mid-line

(g) a standardized method to contour the brachial plexus within non-contrast CT images is provided by Hall WH *et al.*, *Int. J. Radiat. Oncol. Biol. Phys.* **72(5)** (2008) pp. 1362-1367.

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. For IMPT, a robust optimization method that deals with the uncertainties directly during the spot weight optimization to ensure CTV coverage is recommended (this applies to Table 8 as well).

Table 6: Dose descriptions for conventional standard fractionation (5000 cGy in 25 fractions to the intact breast or chest wall; additional 1000 cGy, 1200 cGy, or 1400 cGy to the lumpectomy PTV):

Target Standard Name	**Dose (cGy)**	**Fraction Size** (cGy)	**# of fractions**	**Frequency**	**Dose specification technique**
PTVsb_ Eval	6000 to 6400	200	30 to 32	Daily	Covering 95% of PTVsb_Eval
PTV_Breast_Eval	5000	200	25	Daily	Covering 95% of PTV_Breast_Eval
PTV_Scar_Eval	6000 to 6400	200	30 to 32	Daily	Covering 95% of PTV_Scar_Eval
PTV_CW_Eval	5000 (or 6000 to 6400 if a boost is used)	200	25 (or 30 to 32 if a boost is used)	Daily	Covering 95% of PTV_CW_Eval
PTVn_Sclav	5000	200	25	Daily	Covering 95% of PTVn_Sclav
PTVn_Ax	5000	200	25	Daily	Covering 95% of PTVn_Ax
PTVn_IMN	5000	200	25	Daily	Covering 95% of PTVn_IMN

Table 7: Dose descriptions for conventional hypofractionation to intact breast only (4256 cGy in 16 fractions to intact breast or chest wall); additional 1000 cGy, 1200 cGy, or 1400 cGy to lumpectomy

PTV):

Target Standard Name	Dose (cGy)	Fraction Size (cGy)	# of fractions	Frequency	Dose specification technique
PTVsb_Eval	5256 to 5656	266 primary, 200 boost	21 to 23	Daily	Covering 95% of PTVsb_Eval
PTV_Breast_Eval	4256	266	16	Daily	Covering 95% of PTV_Breast_Eval
PTV_Scar_Eval	5256 to 5656	266 primary, 200 boost	21 to 23	Daily	Covering 95% of PTV_scar_Eval

Table 8: Dose descriptions for Accelerated Partial Breast Irradiation (APBI) (3850 cGy in 10 fractions of 385 cGy delivered twice daily with a minimum of 6 hours between fractions daily **OR** APBI 2700-3000 cGy in 5 fractions 540-600 cGy delivered daily or every other day) **OR** Partial Breast Irradiation (PBI) 4000 cGy in 15 fractions daily.

Target Standard Name	Dose (cGy)	Fraction Size (cGy)	# of fractions	Frequency	Dose specification technique
PTVsb_Eval (option 1)	3850	385	10	Twice daily	Covering 95% of PTVsb_Eval
PTVsb_Eval (option 2)	2700-3000	540-600	5	Daily or every other day	Covering 95% of PTVsb_Eval
PTVsb_Eval (option 3)	4000	267	15	Daily	Covering 95% of PTVsb_Eval

Table 9: Whole Breast dose descriptions for ultra-hypofractionation to intact breast only (2600 cGy in 5 fractions to intact breast); additional 1000 cGy/ 5 fractions sequential optional boost to lumpectomy PTV)

Target Standard Name	Dose (cGy)	Fraction Size (cGy)	# of fractions	Frequency	Dose specification technique
PTV_Breast_Eval	2600	520	5	Daily	Covering 95% of PTV_Breast_Eval
PTVsb_Eval (without boost)	2600	520	5	Daily	Covering 95% of PTVsb_Eval
PTVsb_Eval boost (Optional)	1000	200	5	Daily	Covering 95% of PTVsb_Eval

5.2.7 Compliance criteria

The compliance dosimetric 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.

The nomenclatures for the dosimetric criteria, including volume receiving certain dose (Vx, x is certain dose), dose covering certain volume (Dx, x is certain volume), as well as minimum, maximum, and mean dose, that are used in the following tables, follow AAPM TG263 (Mayo CS, et al., Int. J. Radiat. Oncol. Biol. Phys. 100(4) (2018) pp. 1057-1066) recommendations, and are briefly described in Appendix A.

Normalization of Dose: The plan is normalized such that 95% of the PTV_Breast_Eval or PTV_CW_Eval volume receives at least 95% of prescription dose of 5000 cGy.

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

Target Volume Constraints and Compliance Criteria

Table 10: Target volume constraints and compliance criteria

Name of Structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Notes (Please remove this column when notes are not needed)
Whole breast irradiation without boost				
PTVsb_Eval	D95%[%]	>=95%	>=90%	excludes boost dose
PTV_Breast_Eval	D95%[%]	>=95%	>=90%	excludes boost dose
PTV_Breast_Eval	D5%[%]	<=110%	<=115%	excludes boost dose
PTV_Breast_Eval	D7%[%]	<=105%	<=110%	excludes boost dose
PTV_Breast_Eval	D0.03cc[%]	<=115%	<=120%	excludes boost dose
PTV_Breast_Eval (2600 cGy/5Fx only)	D0.03cc[%]	<=110%	<=112%	excludes boost dose
Whole breast irradiation with sequential or concomitant boost COMPOSITE plan				
PTVsb_Eval	D95%[%]	>=95%	>=90%	includes boost dose
PTVsb_Eval	D0.03cc[%]	<=115%	<=120%	includes boost dose
PTV_Breast_Eval	D95%[%]	>=95%	>=90%	excludes boost dose
PTV_Breast_Eval	D30%[%]	<=100%	<=105%	includes boost dose
PTV_Breast_Eval	D50%[%]	<=108%	<=112%	includes boost dose
PTV_Breast_Eval	D0.03cc[%]	<=115%	<=120%	includes boost dose
Accelerated Partial Breast Irradiation or Partial Breast Irradiation				
PTVsb_Eval	D95%[%]	>=95%	>=90%	
PTVsb_Eval	D5%[%]	<=105%	<=110%	

PTVsb_Eval	D0.03cc[%]	<=115%	<=120%	

Normal Structure Constraints and Compliance Criteria

Conventional standard fractionation (5000 cGy in 25 fractions to intact breast or chest wall):

Table 11: Example set of constraints and compliance criteria for normal structures using conventional standard fractionation, if left side breast is treated

Name of Structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Endpoint/Notes (Please remove this column when notes are not needed)
Lung_L	D15%[cGy]	<=2000 cGy	<=2500 cGy	RTOG 1005
Lung_L	D35%[cGy]	<=1000 cGy	<=1200 cGy	RTOG 1005
Lung_L	D50%[cGy]	<=500 cGy	<= 600 cGy	RTOG 1005
Lung_R	D10%[cGy]	<=500 cGy	<=700 cGy	RTOG 1005
Breast_R	D0.03cc[cGy]	<=310 cGy	<=500 cGy	BR007
Breast_R	D5%[cGy]	<=186 cGy	<=310 cGy	BR007
Heart	D5%[cGy]	<=2000 cGy	<=2500 cGy	RTOG 1005
Heart	D30%[cGy]	<=1000 cGy	<=1200 cGy	RTOG 1005
Heart	Mean[cGy]	<=200 cGy	<=300 cGy	BR007

Per Protocol range is excluded from Variation Acceptable range.

Table 12: Example set of constraints and compliance criteria for normal structures using conventional standard fractionation, if right side breast is treated

Name of Structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Endpoint/Notes (Please remove this column when notes are not needed)
Lung_R	D15%[cGy]	<=2000 cGy	<=2500 cGy	RTOG 1005
Lung_R	D35%[cGy]	<=1000 cGy	<=1200 cGy	RTOG 1005
Lung_R	D50%[cGy]	<=500 cGy	<=600 cGy	RTOG 1005
Lung_L	D10%[cGy]	<=500 cGy	<=700 cGy	RTOG 1005
Breast_L	D0.03cc[cGy]	<=310 cGy	<=500 cGy	BR007
Breast_L	D5%[cGy]	<=186 cGy	<=310 cGy	BR007
Heart	D5%[cGy]	<=2000 cGy	<=2500 cGy	RTOG 1005
Heart	D10%[cGy]	<=1000 cGy	<=1200 cGy	RTOG 1005
Heart	Mean[cGy]	<=100 cGy	<=200 cGy	BR007

Conventional hypofractionation (4256 cGy in 16 fractions to intact breast only):

Table 13: Example set of constraints and compliance criteria for normal structures using conventional hypofractionation, if left side breast is treated

Name of Structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Endpoint/Notes (Please remove this column when notes are not needed)
Lung_L	D10%[cGy]	<=1600 cGy	<=2100 cGy	BR008
Lung_L	D15%[cGy]	<=800 cGy	<=900 cGy	BR008
Lung_L	D25%[cGy]	<=400 cGy	<=500 cGy	BR008
Lung_R	D10%[cGy]	<=400 cGy	<=500 cGy	BR007
Breast_R	D0.03cc[cGy]	<=240 cGy	<=340 cGy	BR007
Heart	D5%[cGy]	<=1600 cGY	<=2000 cGy	BR007
Heart	Mean[cGy]	<=160 cGy	<=320 cGy	BR007

Table 14: Example set of constraints and compliance criteria for normal structures using conventional hypofractionation, if right side breast is treated

Name of Structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Endpoint/Notes (Please remove this column when notes are not needed)
Lung_R	D10%[cGy]	<=1600 cGy	<=2100 cGy	BR008
Lung_R	D15%[cGy]	<=800 cGy	<=900 cGy	BR008
Lung_R	D25%[cGy]	<=400 cGy	<=500 cGy	BR008
Lung_L	D10%[cGy]	<=400 cGy	<=500 cGy	BR007
Breast_L	D0.03cc[cGy]	<=240 cGy	<=340 cGy	BR007
Heart	Dmax[cGy]	<=1600 cGy	<=2000 cGy	BR007
Heart	Mean[cGy]	<=80 cGy	<=160 cGy	BR007

Table 15: Example set of constraints and compliance criteria for normal structures using **APBI accelerated partial breast irradiation**, **(3850 cGy in 10 fractions BID),** 3D conformal or IMRT techniques permitted

Name of Structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Endpoint/Notes (Please remove this column when notes are not needed)
Ipsilateral: Lung_L or Lung_R	D15%[cGy]	<=1155 cGy	<=1348 cGy	NSABP B39/RTOG0413 BR007
Contralateral:	D15%[cGy]	<=192 cGy	<=385 cGy	NSABP B39/RTOG0413

Lung_L or Lung_R				BR007
Uninvolved ipsilateral breast: Breast-PTVsb	D50%[cGy] D30%[cGy]	<=1925 cGy <=3850 cGy	<=2118 cGy <=4043 cGy	BR008
Contralateral: Breast_L or Breast_R	D0.03cc[cGy]	<=115 cGy	<=308 cGy	BR007
Heart (right sided tumor)	D5%[cGy]	<=192 cGy	<=385 cGy	NSABP B39/RTOG0413 BR007
Heart (left sided tumor)	D40%[cGy]	<=192 cGy	<=385 cGy	NSABP B39/RTOG0413 BR007
Heart (left sided tumor)	Mean [cGy]	<=80 cGy	<=150 cGy	BR007

Table 16: Example set of constraints and compliance criteria for normal structures using **APBI accelerated partial breast irradiation (2700-3000 cGy in 5 fractions daily or every other day),** 3D conformal or IMRT techniques permitted

Name of Structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Endpoint/Notes <u>(Please remove this column when notes are not needed)</u>
Ipsilateral: Lung_L or Lung_R	D15%[cGy]	<= 900 cGy	<=1050 cGy	BR008 (no variation acceptable in the protocol)
Contralateral: Lung_L or Lung_R	D15%[cGy]	<=150 cGy	<=300 cGy	BR008 (no variation acceptable in the protocol)
Uninvolved ipsilateral: Breast_PTVsb	D50%[cGy] D30%[cGy]	<=1500 cGy <=3000 cGy	<=1650 cGy <=3150 cGy	BR008 (no variation acceptable in the protocol)
Contralateral: Breast_L or Breast_R	D0.03cc[cGy]	<=90 cGy	<=240 cGy	BR008 (no variation acceptable in the protocol)
Heart (right sided tumor)	D5%[cGy]	<=150 cGy	<=300 cGy	BR007
Heart (left sided tumor)	D40%[cGy]	<=150 cGy	<=300 cGy	BR008 (no variation acceptable in the protocol)
Heart (left sided tumor)	Mean [cGy]	<= 60 cGy	<=110 cGy	BR007

Table 17: Example set of constraints and compliance criteria for normal structures using whole breast irradiation with 2600 cGy in 5 fractions with 3D conformal or IMRT techniques permitted

Name of Structure	Dosimetric parameter	Per Protocol	Variation Acceptable	Endpoint/Notes (Please remove this column when notes are not needed)
Ipsilateral: Lung_L or Lung_R	D15%[cGy]	<=800 cGy	<=930 cGy	FAST-Forward BR007
Contralateral: Lung_L or Lung_R	D10%[cGy]	<=500 cGy	<=630 cGy	FAST-Forward
Contralateral: Breast_L or Breast_R	D0.03cc[cGy]	<=310 cGy	<=500 cGy	BR008
Contralateral: Breast_L or Breast_R	D5%[cGy]	<=186 cGy	<=310 cGy	BR008
Heart (right sided cancer)	D5%[cGy]	<=150 cGy	<=280 cGy	BR007
Heart (Left sided cancer)	D5%[cGy]	<=700 cGy	<=830 cGy	FAST-Forward BR007
Heart (left sided cancer)	D30%[cGy]	<=150 cGy	<=280 cGy	FAST-Forward BR007
Heart (left sided cancer)	Mean [cGy]	<=50 cGy	<=100 cGy	BR007

For the evaluation of a proton plan, robustness evaluation using 5 mm setup uncertainty and 3.5% range uncertainty is highly recommended. At a minimum, the evaluation should be performed both on an individual beam basis to insure adequate proximal and distal coverage and on the summation of all beams to ensure PTV coverage.

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 given as an example

1. Spinal Cord
2. Heart
3. CTV
4. Ipsilateral lung
5. PTV
6. Breast
7. Contralateral lung
8. Contralateral breast

- Required algorithms
(Convolution/Superposition, Monte Carlo, etc…)

Acceptable choices of algorithm are listed at http://rpc.mdanderson.org/rpc/Services/Anthropomorphic_%20Phantoms/TPS%20-%20algorithm%20list%20updated.pdf. Any algorithm used for this study must be credentialed by IROC Houston.

The calculation of photon dose deposition may be performed using convolution-algorithm techniques, superposition techniques, or Monte Carlo techniques. The calculation of electron dose deposition may be performed using pencil-beam (PB) or Monte Carlo algorithms.

For Convolution/Superposition type algorithms, dose should be reported as computed inherently by the given algorithm. For Monte Carlo or Grid Based Boltzmann Solver algorithms, conversion of Dm (dose-to-medium) to Dw (dose-to-water) should be avoided. Dm, computed inherently by these algorithms, should be reported. These principles hold for Pencil Beam type algorithms and for homogeneous dose calculations when allowed for a clinical trial (e.g., conical collimators in stereotactic radiosurgery).

For proton therapy, MC or equivalent algorithms should be used for dose reporting, due to the PB algorithm dose error caused by the use of range shifter and the existence of relatively large air gap.

- Primary dataset for dose calculation

The primary CT dataset for dose calculation may be acquired via the following techniques:

- free-breathing with no motion management;
- breath-hold (e.g. DIBH);
- gated CT acquisition;
- 4DCT acquisition, from which an average intensity pixel CT (AveIP) is generated; note that Maximum Intensity Pixel (MIP) generated images from 4DCTs may not be used as the primary dose calculation dataset.

If contrast is present during the treatment planning CT acquisition, the density of the contrast should be overridden to a representative background electron density.

-Dose matrix resolution

Dose grid size should be ≤ 3 mm in all directions.

The TPS may assign electron densities or physical densities for each voxel in the volumetric planning image, to account for tissue density for beam attenuation and dose calculation. The following techniques may be used for density assignment:

- Voxel-by-voxel assignment using an appropriate IVDT
- Assignment of specific ROIs to specific uniform density values appropriate to the ROI; examples include density overrides to correct for image artifacts (e.g. due to the presence of highly-attenuating materials), to remove from the image any contrast agent that was present during simulation, and the assignment of ROIs delineated in an MR planning image to an appropriate density (“synthetic CT”)

An accurate accounting of the variable tissue density within the planning image shall be done within the TPS. For CT-based planning, a CT-number-to-electron-density or CT-number-to-physical density table shall be measured within the institution’s imaging system, and reviewed and credentialed as appropriate. For MR-based planning, an atlas-based “synthetic CT” image with appropriate densities assigned to all regions of interest may be obtained from the planning MR image.

Planning techniques for whole breast irradiation, which may include a boost (sequential or simultaneous) to a post-lumpectomy PTV as well as coverage of regional lymph nodes for more-advanced disease, include the following:

- Opposed open tangent fields (from the medial and lateral directions) designed using a 3DCRT planning technique. Field aperture shapes may be determined using either cast blocks or multileaf collimators. The beam directions and aperture shapes shall be designed so that the posterior borders of the open tangent fields align with each other. The superior or inferior borders of the open tangent fields may be allowed to diverge, but if the tangent fields are to be matched to a dedicated supraclavicular field, the superior borders of the open tangent fields must align with each other. The intensity profile of the open tangent fields may be modified using either wedges (physical, motorized, or virtual/dynamic) or compensators. For younger patients, virtual wedges should be used if possible, to minimize scatter dose to the contralateral breast. Modulation may also be achieved using forward-planned partially-blocked sub-fields (the so-called field-in-field technique). If this technique is used, ensure that the calculation point for each field is within a uniform-tissue region of sufficient cross-sectional area; this area will depend upon the accuracy of the beam model within the TPS.
- Inverse-planned fields using static-field IMRT (step-and-shoot or sliding window) or modulated arc-therapy techniques (IMAT, VMAT, or tomotherapy). Segment aperture shapes may be determined using either multileaf collimators or compensators. Photon beam energies of 10 MV or lower are preferred, so as to minimize neutron dose to the patient; tangential-beam IMRT using energies greater than 10 MV is acceptable given that the monitor units per segment are similar to that achieved using the field-in-field technique. If 10 MV photons are planned, a beam spoiler may be used to compensate for the otherwise greater (approximately 2 cm) buildup depth from the skin surface to d_{max}). Static-field IMRT plans should start with tangent-field geometries; additional fields with different beam angles may be added, but the plan should minimize entrance dose to the lungs, heart, and contralateral breast. For modulated arc-therapy IMRT techniques, the arc range should be chosen so as to avoid entrance dose to the lungs, heart, or contralateral breast. The institution must be credentialed for IMRT, including its plan verification and QA techniques.

If a boost treatment to a post-lumpectomy PTV is planned, the field apertures should be extended 5 mm beyond the edges of the PTV within the BEV. PTV boost fields may be planned and delivered using 3DCRT or IMRT external beam therapy, enface electron beams, proton beams (3DCPT or IMPT), brachytherapy (provided that the institution is credentialed to use the specific brachytherapy technique), intraoperative electron or HDR techniques, or cobalt teletherapy (e.g Xcision GammaPod).

Couch attenuation should be considered in planning with treatment couch appropriately inserted and electron density assigned. Breast board, if in the beam path, should be included in the dose calculation also.

For proton therapy, enface beam angles should be used. For 3DCPT using passive scattering or uniform scanning, customized apertures or MLC and compensators should be used to shape the fields laterally and distally. When matched fields are needed due to the larger target size, matchlines should be shifted throughout the course of radiotherapy to minimize hot and cold spots at the field junctions. A minimum of 2 matchlines, separated by ≥ 1 cm, is recommended. Range shifters may be used for IMPT plans to make adjustment of the proton range. Robust optimization with 5 mm setup uncertainty and 3.5% range uncertainty on CTV is strongly recommended. Single-field optimization (SFO) in which each field is optimized to deliver a uniform dose to the target volume is recommended. Multi-field optimization (MFO) or intensity modulated proton therapy (IMPT) will be allowed when deemed necessary, for example, using treating around technique on a tissue expander case. At least weekly CBCT or bi-weekly QA CT is recommended to evaluate anatomy change and potential impact to the dose distribution. Adaptive replan should be performed when the dose distribution deviates from the protocol accepted criteria.

When treating implant or tissue expander cases using proton therapy, the CT imaging artifact must be carefully addressed by contouring and assigning the corresponding relative stopping power (RSP). The implant made from silicone should be contoured and overridden with proper density and relative RSP. For tissue expander cases, when proton beam is used to treat through the high-Z materials, the high-Z material must be contoured with the dimensions matched to the vendor's specification and the corresponding RSP must be assigned. When treating around technique (no beam treating through the high-Z material inside the tissue expander) is used, avoid structure of the high-Z material with adequate margin must be used.

-List treatment planning recommendations and give link to FAQs

5.2.9 Patient specific QA

- Describe technique and give Gamma pass rate recommendation

Any patient-specific QA that needs to be acquired should follow institutional guidelines.

For IMRT, VMAT, or proton plans (the latter being an option for post-lumpectomy boost irradiation), patient specific QA is highly recommended. Any patient-specific QA performed should follow institutional guidelines. The recommended patient specific QA criterion is for 95% (tolerance limits) or 90% (action limits) of the comparison points to pass a ±3%/2mm and 10% dose threshold Gamma Index analysis per AAPM Task Group 218 guidelines (Miften et al Med Phys 45: e53-e83, 2018).

For passive scattered or uniform scanned beam plans that utilize a match or patch field, patient specific QA must be performed with the compensator.

For forward-planned EBRT delivery, verification of the MU calculation for each field within the TPS shall be performed prior to administration of the first fraction. Heterogeneity corrections shall be used for the MU verification calculations if they were incorporated into the TPS MU calculation. Acceptable differences between the TPS and verification calculations for MU may be determined by the institution, subject to protocol credentialing and approval. The TPS MU calculation takes precedence, and shall only be modified to match the verification MU if during the course of treatment the patient thickness along a given beam direction is observed to change enough to affect a > 5% difference in the dose contributed by that beam.

For inverse-planned EBRT delivery, although an automated MU verification calculation may be permitted subject to protocol credentialing and approval, a direct measurement of the dose distribution from the designated treatment system shall be performed prior to delivery of the first fraction. All components of the inverse-plan verification technique, including the planning system, treatment machine, and detector hardware and analysis procedure, shall be credentialed according to guidelines established by IROC-Houston for protocols utilizing inverse planning.

In vivo dosimetry may be used to verify patient doses in the near surface region (such as dose to the chestwall beneath bolus).

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.

Verification Prior to the First Fraction

Prior to delivery of the first fraction, the position of the patient relative to the radiation source shall be verified through either planar radiographs or volumetric images. Target-to-skin distance (TSD) measurements shall be performed to compare with reference values obtained by the TPS. Delivering the first fraction on the same day as the above pre-treatment verification measurements is optional.

Verification during Subsequent Fractions

For treatments prescribed for five or more consecutive-daily fractions, imaging for position verification shall be performed prior to fraction delivery once every five fractions. For treatments prescribed fewer than five consecutive-daily fractions, or treatments prescribed three or fewer fractions per calendar week, position-verification imaging shall be performed prior to every fraction delivery.

Daily IGRT (KV/KV orthogonal, CBCT or surface imaging) is required for proton therapy.

Required verification imaging techniques include the following:

- Planar imaging (port films), for treatment fields and/or orthogonal fields; treatment-field portal imaging is applicable only for forward-planned EBRT; lateral orthogonal fields must be proximal to the ipsilateral breast; port films that are incident through the treatment couch should be avoided if possible; either kilovoltage or megavoltage planar films are acceptable

Acceptable verification imaging techniques include the following:

- Fluoroscopy (either kilovoltage or megavoltage) may be used for motion-correlated delivery techniques
- Fan-beam kVCT (CT-on-rails)
- Fan-beam MVCT (TomoTherapy Hi-Art or Accuray Radixact)
- On-board cone-beam CT (kVCBCT or MVCBCT)
- Tomosynthesis (either kV or MV)
- Ultrasound (for post-lumpectomy boost-volume treatments)
- Surface imaging

For photon therapy, TSD measurements shall be performed prior to fraction delivery once every five fractions. If a verification image is acquired during the same session, the TSD measurement shall be done following patient repositioning following the verification image, but prior to the fraction delivery.

Image-guided Patient Position Refinement

Prior to fraction delivery, the positioning of the patient may be refined using any of the above-listed verification imaging techniques. A reference image from the TPS shall be used for comparison with the verification image. Patient position refinement may either be translational only (along the three cardinal directions: lateral, longitudinal, or vertical), or it may include rotational corrections (pitch, roll, and yaw). The basis of the IGRT alignment shall be determined prior to the first fraction delivery and documented in the patient's electronic medical record. Criteria for internal review of the repositioning shall be established by the institution and subject to review and credentialing by the protocol. If required by the protocol, verification imaging following the patient repositioning shall be acquired, the frequency of which shall be determined by the protocol.

The following information should be provided for Localization guidance

- Will simple isocenter localization technique be used at 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-xray, electromagnetic localization, optical surface imaging, 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 mm is not recommended)
- Recording of shift information must be provided for the IGRT credentialing process
- Other

Management of Radiation Dose to the Patient from IGRT

NRG Oncology is concerned about the estimated irradiation 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 studies are done for patients with severe set up problems (e.g. requiring frequent corrections that are larger than the PTV margins). For such patients, it is recommended that they be re-planned and treated with larger margins after the first week of treatment.

If possible, verification imaging dose shall be calculated or estimated within the TPS. An action level for excess dose due to unplanned verification imaging, as well as the measures to take if the action level is reached or exceeded, shall be established by the institution and subject to approval by the protocol.

5.2.11 Case Review

The Principal Investigator(s), XXX, MD will perform ongoing remote RT Quality Assurance Review after cases enrolled have been received at IROC Philadelphia-RT.

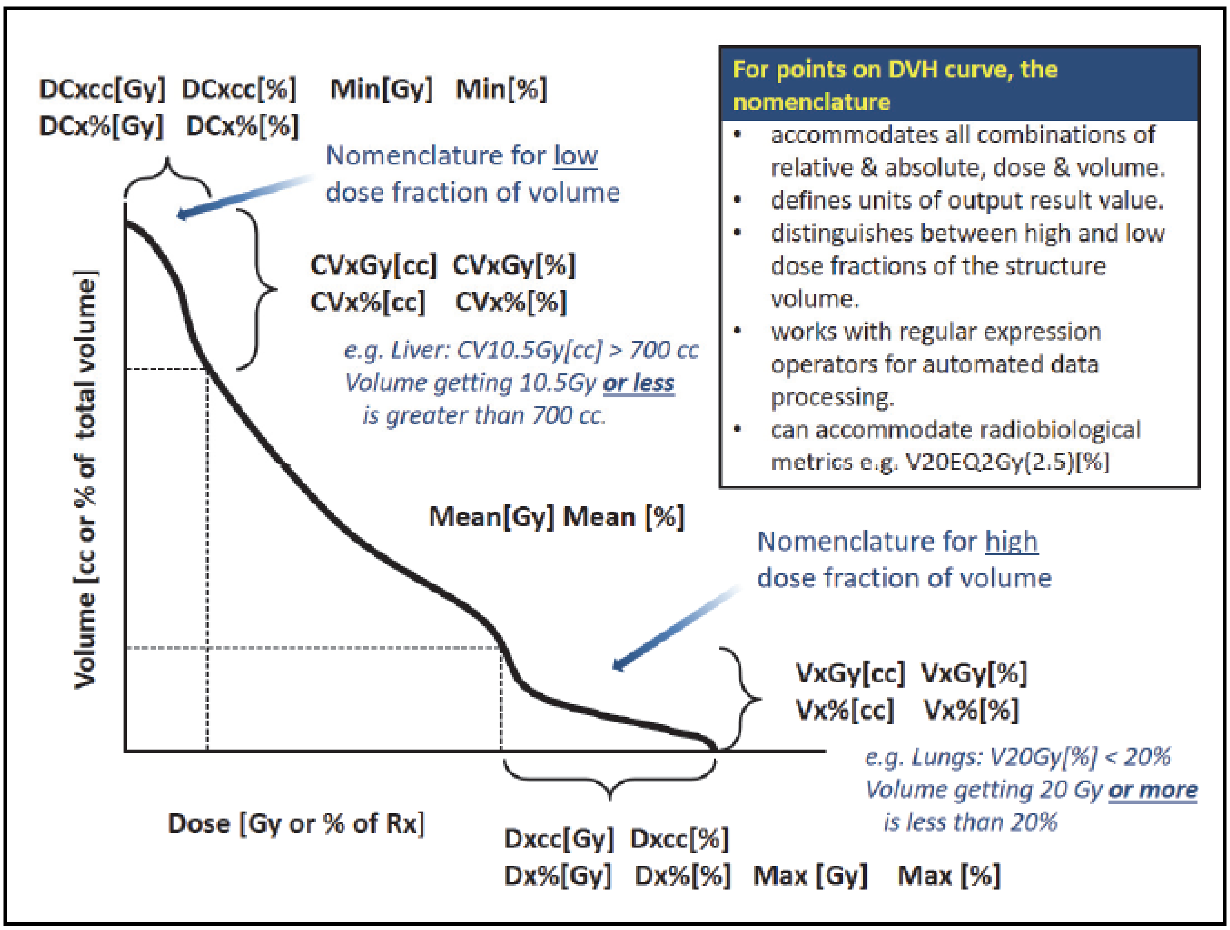
APPENDIX A
RECOMMENDATIONS FOR DOSE VOLUME HISTOGRAM METRICS

AAPM TG263 recommendations for dose volume histogram metrics are followed:

- Measurement (output) type is specified at the beginning of the string, units or label for what is measured are specified at the end of the string, enclosed in square brackets, e.g., VxcGy[cc] means the volume (V) is measured with its unit specified in cc and placed in [].
- Units or label for where on the DVH curve the point is measured (input) is specified after the measurement type but before the output unit, e.g., VxcGy[cc] means the measurement point is for dose ≥ x cGy.
- Volume of cold dose is specified with C in front of volume. E.g., CVxcGy means the volume receiving dose ≤ x cGy.

Figure 1 illustrates the TG263 recommended DVH nomenclature with absolute dose unit still in Gy. Absolute dose unit has been changed to cGy in this protocol.

Figure 1. Illustration of standardized DVH nomenclature specifying input and output units.



The following explains the DVH metrics that are frequently appeared in BR007 dosimetric criteria:

- VxcGy [cc], VxcGy [%], Vx%[cc], Vx%[%]: Volume [cc or %] receiving Dose x [cGy, or %] or more.

The dose values can be either absolute (xcGy) or relative (% of prescription dose), and the volume values can be also either absolute (cc) or relative (% of volume). For example, Lung_L V2000cGy[%] ≤ 15% means the volume of Lung_L receiving dose of 2000 cGy or more should be less than or equal to 15% of the total Lung_L volume.

- Dxcc[cGy], Dxcc[%], Dx%[cGy], Dx%[%]: Dose [cGy or %] covering Volume [cc or % of total volume].

  The volume values (x) can be either absolute (cc) or relative (% of the corresponding structure volume), and the dose values (D) can be also either absolute (cGy) or relative (% of prescription dose). For example, Breast_R D0.03cc[cGy] ≤ 310 cGy means the hot dose covering 0.03 cc of Breast_R should be less than or equal to 310 cGy.

- Min[cGy], Min[%]: Minimum dose expressed in cGy or a percentage of the prescription dose. It is often defined to D99%[cGy] or D99%[%] since point dose may be TPS and dose calculation grid dependent. This is equivalent to DC1%[cGy] or DC1%[%].
- Max[cGy], Max[%]: Maximum dose expressed in cGy or a percentage of the prescription dose. It is often defined as D0.03cc[cGy] or D0.03cc[%] for the same reason as mentioned in Minimum dose.
- Mean[cGy] or Mean[%]: Mean dose expressed in cGy or a percentage of the prescription dose.
- R100%: Ratio of 100% isodose volume over structure volume [SBRT only].
- R50%: Ratio of 50% isodose volume over structure volume [SBRT only].

While all above quantities can be used, it is recommended to use D values (Dxcc[cGy], Dxcc[%], Dx%[cGy], Dx%[%], Min[cGy], Min[%], Max[cGy], Max[%], Mean[cGy], Mean[%]) instead of V values (VxcGy[cc], VxcGy[%], Vx%[cc], Vx%[%]) when possible.