NRG ONCOLOGY

Advancing Research. Improving Lives.™

NRG ONCOLOGY PROTOCOL DEVELOPMENT TEMPLATE FOR RADIATION THERAPY

DISEASE SITE: Brain
SUB-COMPONENT: SRS

Authors & Affiliations:

Yunfeng Cui, Ph.D., Duke University Medical Center, Durham, NC
Tomi Ogunleye, M.S., Northside Hospital, Cumming, GA
John Kirkpatrick, M.D., Ph.D., Duke University Medical Center, Durham, NC
Ying Xiao, Ph.D., University of Pennsylvania, Philadelphia, PA
Paul Sperduto, MD, MPP, Minneapolis Radiation Oncology PA, Waconia, MN
Fang-Fang Yin, Ph.D., Duke University Medical Center, Durham, NC

Reviewers &Affiliations:

David Gladstone, Sc.D., Dartmouth-Hitchcock Medical Center, Lebanon, NH
Robert Wallace, Ph.D., Cedars-Sinai Medical Center, Los Angeles, CA
Jason Sohn, Ph.D., Case Western University, Cleveland, OH

Maintained By: NRG Medical Physics Subcommittee
NRG Radiation Oncology Committee

Version 1: 06-13-2016

CIRO
Center for Innovation in Radiation Oncology
NRG Oncology

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**.**

5.2 Radiation Therapy

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 SRS head phantom irradiation credentialing and the IGRT credentialing) should be explicitly specified in the protocol.

5.2.1 Treatment Technology

List allowed Treatment Modalities (including energy and beam modifiers): photons, protons, …, also MLC, leaf width, cone types, etc.

Example: This protocol requires photon treatment. GammaKnife or linear accelerator-based treatments with nominal x-ray energy of 6MV or greater (including isocentric conical collimators, MLC, or linear accelerators mounted on robotic arms) are allowed. The treatment machines must be commissioned for small field sizes. Credentialing for SRS head phantom irradiation from IROC Houston is mandatory. 3D-CRT (including static and dynamic MLC arcs), IMRT techniques (including Tomotherapy and VMAT) are allowed.

5.2.2 Immobilization

Describe recommended patient setup and immobilization methods which may meet optimal SRS accuracy. The protocol should state that the immobilization method used should limit the motion within certain degree (for example, <1 mm and <1◦).

Example: Proper immobilization is critical for this protocol. Patient setup reproducibility must be achieved using appropriate clinical devices. Both invasive frame-based immobilization and non-invasive thermoplastic mask based immobilization are allowed.

5.2.3 Simulation Imaging

This subsection should include information about the extent of CT imaging, field-of-view (FOV), 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.

Example: Contiguous CT slices of 1.25 mm slice thickness or less should be obtained. CT scan should cover from top of head to bottom of skull. Contrast enhancement during CT-simulation will be permitted if there are no MR images available for target delineation. 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. To avoid this issue, two scans can be ordered with and without contrast.

This subsection should also describe additional image modalities, image registration/fusion, and follow-ups. Please remove this part if it does not apply to your protocol.

Example: MR imaging is strongly encouraged for target delineation. FDG-PET/CT images are also recommended to be fused together if available. Image fusion must be performed by a qualified medical physicist and reviewed by the attending physician.

Specific requirement regarding MRI sequences to be acquired can be listed here.

Example: Contrast enhanced T1-weighted MR and Spoiled Gradient Echo (3D SPGR – the term used by GE scanner; other scanners use different name) images should be used for target volume delineation.

5.2.4 Definition of Target Volumes and Margins

Note: Target names should follow the naming convention detailed in the table below. Each target will be named anatomically for the lobe of the brain along with "Left or Right" denoting in which hemisphere the target is located. Following the target type (GTV, CTV, or PTV) will be a number representing the order of the targets (i.e. first target, second target, …). All structures must be named for digital RT data submission as listed in the table below. 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. Example target names are: GTV1_Frontal_R, CTV3_Cerebellum_L, PTV7_Brainstem (note: for Brainstem target, no Left or Right is required in the target name).

Target names:

GTV(1-9)_	Frontal	_L
CTV(1-9)_	Parietal	_R
PTV(1-9)_	Cerebellum	
	Temporal	
	Occipital	
	Brainstem	(No Lateral)

Detailed Specifications

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

GTV, CTV, and PTV should be all defined. If CTV is the same as GTV, then state CTV=GTV. Also state how GTV should be defined.

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

GTV: The GTV is defined as the enhancing metastasis on a gadolinium enhanced 3D SPGR MRI scan (Description of GTV delineation to be written by physician PI of the study).

CTV: CTV is defined as identical to GTV.

PTV: The PTV is defined as the CTV plus a symmetrical 1.0mm margin.

5.2.5 Definition of Critical Structures

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.

Standard Name	Description	Importance **(Required/Required when applicable/Optional)**
Brain	Brain	Optional
BrainStem	Brainstem	Required
Cochlea_L	Left cochlea	Optional
Cochlea_R	Right cochlea	Optional
OpticChiasm	Chiasm	Required when applicable
OpticNrv_L	Left optical nerve	Required when applicable
OpticNrv_R	Right optical nerve	Required when applicable
Eye_L	Left eye	Required
Eye_R	Right eye	Required
Lens_L	Left lens	Required when applicable
Lens_R	Right lens	Required when applicable
Orbit_L	Left orbit	Required when applicable
Orbit_R	Right orbit	Required when applicable

Detailed Specifications

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

5.2.6 Dose/Volume 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.

Example:

SRS for unresected brain metastases:
PTVs with maximum dimension <1.0 cm receive 24 Gy
PTVs with maximum dimension ≥1.0 cm and <2.0 cm receive 20 Gy
PTVs with maximum dimension ≥2.0 cm and <3.0 cm receive 18 Gy

SRS for surgical bed (surgical cavity volume):
PTVs < 4.2 cc receive 20 Gy
PTVs ≥ 4.2 cc and < 8.0 cc receive 18Gy
PTVs ≥ 8.0 cc and < 14.4 cc receive 17 Gy
PTVs ≥ 14.4 cc and < 20 cc receive 15 Gy
PTVs ≥ 20 cc and < 30 cc receive 14 Gy
PTVs ≥ 30 cc and < 5cm in maximum dimension receive 12 Gy

The dose is prescribed to the isodose line encompassing at least 99% of the PTV.

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 [Gy, or %]
Dxcc[Gy], Dxcc[%], Dx%[Gy], Dx%[%]: Dose [Gy or %] to Volume [cc or % of total volume]
Minimum dose is defined to D99%[Gy] or D99%[%]
Maximum dose is defined as D0.03cc[Gy] or D0.03cc[%]
Mean[Gy] or Mean[%]: Mean dose in Gy or %
Conformity Index (CI or R100%): Ratio of prescription isodose volume over the target volume, i.e. $CI=V_{Rx}/V_{PTV}$, where V_{Rx} is the prescription isodose volume and V_{PTV} is the volume of PTV.

R50%: Ratio of 50% prescription isodose volume over the target volume (R50% defines dose falloff outside the target)
Heterogeneity index (HI): The ratio of highest dose received by 5% of PTV to lowest dose received by 95%of PTV, i.e. HI=$D_{5\%}$[Gy]/$D_{95\%}$[Gy]
Coverage=(Volume of PTV receiving prescription dose)/V_{PTV}

Normalization of Dose: Example: The plan is normalized such that at least 99% of each PTV volume receives prescription dose.

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

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)
PTV	D99%[%]	100%	95% to 105%	
	D0.03cc[%]	≤120%	≤125%	
	CI (see table below)			

Per Protocol range is excluded from Variation Acceptable range.

Criteria for certain dosimetry parameters (e.g. CI) should account for differences in target size, treatment technology, etc, and should be specified for each different subcategories.

Example: Criteria for Conformity Index (CI)

Volume of target (cc)	Per Protocol	Variation Acceptable	Deviation Unacceptable
≥ xx	≤ 1.5	≤ 1.8	> 1.8
< xx and ≥ yy	≤ 1.7	≤ 2.0	> 2.0
<yy	≤ 2.0	≤ 2.4	> 2.4

Normal Structure Constraints and Compliance Criteria

Name of Structure	Dosimetric	Per Protocol	Variation	Endpoint/Notes

	parameter		Acceptable	(Please remove this column when notes are not needed)
BrainStem	D0.03cc[Gy]	< 14Gy	< 14Gy	
	D99%[Gy]	< 12Gy	< 12Gy	
OpticChiasm, OpticNrv	D0.03cc[Gy]	< 8Gy	< 8Gy	

Per Protocol range is excluded from Variation Acceptable range.

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			
Interruptions			

5.2.8 Treatment Planning Priorities and Instructions

- Critical Structure and Target optimization priorities (importance weights) 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. PTV1, PTV2, …
2. BrainStem
3. OpticChiasm, OpticNrv_L, OpticNrv _R
4. Eye_L, Eye_R
5. Other

- 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. Besides the algorithms listed, the pencil beam algorithm is also allowed in this protocol. Any algorithm used for this study must be credentialed by IROC Houston.

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).

- Primary dataset for dose calculation
Planning CT image is the primary dataset for dose calculation. In case MR image is used for dose calculation, a method of correcting image distortion and tissue density has to be applied to get accurate body contour and heterogeneity corrections. Periodic phantom QA is a must to verify its linearity.

-Dose matrix resolution
Dose grid size should be ≤ 1.25 mm in all directions.

-List treatment planning recommendations and give link to FAQs
Protocol specifies what types of treatment/planning techniques are allowed in the protocol. Potential techniques include 3D conformal beams, static MLC arcs, dynamic conformal MLC arcs, cone-based arcs, IMRT, VMAT, GammaKnife, CyberKnife, or combination of different techniques. If any special instruction is needed for planning with certain technique, it should be clearly described in detail in the protocol. For example:

Using single isocenter to treat multiple targets at same time is allowed with VMAT technique (or other published equivalent techniques). By doing so, dosimetric compliance criteria should be evaluated for each target individually. In this case, the mechanical tolerances such as gantry accuracy would need to be tighter than the specs in the TG-142 of AAPM Report if the distance from the isocenter to the target is large.

If any technique needs to go through special credentialing (e.g. dry-run planning), it should be specified in the protocol.

- Evaluation of plan deliverability
Describe required or suggested planning measures to be taken to ensure a plan is deliverable and to embody collision clearance checks prior to treatment process.

5.2.9 Patient specific QA
- Describe technique and give Gamma test parameters in mm and percentage and Gamma pass rate recommendation. Patient specific QA is required for all intensity modulated plans with inverse planning technique. For non-IMRT plans (e.g. GammaKnife, Dynamic Conformal Arc, Cone-based plan), second verification calculation of MU/beam-on time is efficacious.

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

For photon IMRT plans, patient specific QA is mandatory. QA is performed by delivering the plan onto a phantom and measuring the dose using an ion chamber array or other 2D/3D device. Measured dose distribution will be compared to planned dose distribution using a Gamma criterion of 3% dose difference and 3 mm distance to agreement. The pass rate should be at least 90% measured for the entire plan.

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. IGRT should be credentialed by IROC when IGRT is used for patient setup.

The following information should be provided for localization guidance

- For SRS treatment, IGRT is mandatory except for invasive frame based setup on GammaKnife treatment.
- 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, other?
- Image registration techniques: bone as surrogate, fiducial markers, soft tissue, other
- State the frequency for localization checks, e.g. re-imaging after shift, re-imaging after tx
- Give recommendations for correcting (e.g. correcting for linear shifts larger than 1 mm and rotational deviation larger than 0.5°)
- Other including surface tracking systems

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.

Daily Treatment check sheet

Prior to delivery of radiation, develop a verification checklist. The checklist should include collision clearance check for each radiation delivery field, final patient position verification signed by

physician, etc. Therapist and physicist sign off of each step.

5.2.11 Case Review

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