Every patient: PATHOLOGY, RADIOLOGY, LABS

Every patient: OPERATIVE NOTE, unusual PAST Medical History, Pregnancy

\*\*no phenytoin and brain xrt risk of stevens Johnson

BRAIN:

V105% <10%

107% <.03cc (or variation acceptable 110% max)

Keep hotspots in ctv

95% covers 99% (or 95%)

Spinal cord 50

Brainstem 54Gy

Brainstem PRV 55-56Gy

Optic chiasm PRV 54-55Gy

Optic chiasm 54Gy

Optic nerve max 54Gy

Optic nerve PRV 55Gy

Retina 45Gy

Lens max 7Gy

54Gy <23% brain.

Scalp max 40Gy (is possible)

Hippocampus mean <20-30Gy

Volumes of gtv and ctv and ptv:

Kelly self: Gtv 19cc, ctv2cm 154cc, ptv 207cc

George matiossian: gtv1 111cc, ptv1 335cc, ptv2 232cc

Small brain volumes = 75cc

Small tumor size 42-50cc do better

What does imrt versus 3dcrt look like

Wedge pair

General:

No beams through eyes (tomotherapy directional block like SRS)

If laterals tomotherapy direct block like breast

No contralateral brain radiation

Avoid structure 55.8Gy to push hotspots in ptv

46Gy / 60Gy (2Gy)

50Gy (1.67) / 75Gy (2.5Gy)

Grade III anaplastic astrocytoma: 50.4Gy / 9Gy boost (1.8Gy to isocenter)

Gliomatosis cerebri: >=3 lobes of brain. 54Gy instead of 60Gy if too large an area. Reduce margins after 45Gy from 2cm to 0.7cm or even less margin! Reduce dose from 59.4Gy to 55.8Gy. (50-66Gy reported in literature or 50Gy in 20fx of 2-3cm). no difference in 54Gy in MDACC paper. <40yo do better. (could consider whole brain but modern studies don’t do it, most recurrences infield). Emory: 0.5-1.5cm margin and for the GTV2 boost only 0.5cm margin!! Corpus callosum involved 50%

70% of normal brain spared the 54Gy. 54Gy <23% brain.

LOW GRADE GLIOMA ADDITIONAL:

T2 weighted images from postoperative MRI scan

Use preop if biopsy only

ANY T2 abnormality

2cm margin to block edge (no CTV and no PTV, just GTV + 2cm)

No boost volume.

Margins reduced to 1cm around critical structures: pituitary gland, chiasm, brainstem.

Contralateral brain must be less than 36Gy

105% hotspots no hotter.

2 weeks to heal from surgery

Start date 5-6-7 weeks post surgery

Fuse pre and postop mri brain

Mri T1 post and T2 flair within 72 hours

>3 weeks do another mri T1post and T2flair

Supine, thermoplastic mask, bite block

Sequential versus simultaneous integrated boost

T2/Flair postop mri brain inclusive of t1 post and surgical cavity + 2cm

No falx, ventricles, skull.

2cm edema to block edge.

If no T2/flair, then just CTV + 2cm margin.

Boost: T1 post contrast and surgical cavity + 2cm

No ptv beyond bone

Smooth out pixels

OAR (PRV 3-5mm):

“AVOID” structure. Donuts to limit hotspots, etc.

Lens and cervical spine shielded from direct beams

Spinal cord max 45Gy

Brainstem max 54Gy

Optic chiasm (seen on t2 flair) max 54Gy

Optic nerves, left, right max 54Gy

Retina left, right max 45Gy

Brain max 78.7Gy < 5% (105%<5%)

(Brain 54Gy < 25%)

Whole brain mean < 30Gy (30Gy <50-60%)

Lens right, left max < 7Gy

Pituitary/hypothalamus max < 30Gy

Inner ear max <30Gy

Cochlea left, right max < 30Gy

Lacrimal gland max <30Gy

Infratentorial mean <10Gy (<5Gy)

Hippocampus mean < 20-30Gy

Scalp skin 30Gy max (near tumor)

Minimal PTV in Bone (brain +1-2mm, then crop PTV)

EAR right, left, max <30Gy

Max hot spot 105%

1.8Gy to 59.4Gy total

PTV1: 50.4Gy

PTV2 boost: 9Gy

Sequential boost, IMRT

Please keep hotspots in CTVs if possible

Treatment time less than 6 min?

Try to avoid contralateral left brain. i.e. maybe like wedge pair?

Have 30Gy 50% IDL wrap around PTV on right side

No beams through eyes

No beams through spinal cord

Smooth out pixels/postprocessing

Tomotherapy directional block of eyes??

If do concomitant imrt boosts then the 90% isodose line changes.

LOW GRADE GLIOMA

50.4Gy codel (uses temozolomide concurrent so okay to go to lower dose?)

54Gy 9802 (PCV)

100% dose covers 95% PTV

100% PTV covered by 95% dose

Contralateral brain: \*\*no more than 1% of contralateral brain or 1cc of contralateral brain receives more than 30Gy.

TOMODIRECT FOR EYES

PTV: no more than 1% or 1cc of tissue outside of PTV receives more than 110%

Appendix X on codel for low grade glioma: 95% of PTV volume.

Ptv minimum 0.1cc = 90% (4536cGy)

PTV maximum 0.1cc = 110% (5544cGy)

OAR max of 0.03cc for the following (ideally PRV unless tumor close to normal structure than just get the OAR max dose down) (OAR has higher priority than PTV):

PRV spinal cord is 5mm

PRV optics at least 1mm

PRV brainstem at least 1mm

Brainstem 55-60Gy

Optic nerves 54-56Gy

Optic chiasm 54-56Gy

Retina 45-50Gy

Cervical spinal cord 50Gy

Lens 10-15Gy

Other random structures in brain planning:

Parotids <10Gy

Oral cavity/lips/nasal cavity mean <20Gy. 40Gy <1%

Inner/middle ear mean 30Gy, 50Gy<1%

Lens ALARA

**6.0 RADIATION THERAPY**

**6.1 General Requirements**

• Megavoltage machines ≥ 6MV

• SAD ≥ 100 cm

• At least 2 fields, shaped, all fields treated daily; **the use of opposed lateral fields treating significant**

**volumes of uninvolved contralateral normal brain is strongly discouraged**

• 2 or 2.5D *(i.e., coplanar)* or 3D *(i.e., coplanar or noncoplanar)* treatment planning approaches can be

used

• Port films need to be taken per department routine but will not be submitted to RTOG for review.

**6.2 Treatment Volumes**

The target volume is based on the T2 weighted images from the postoperative MRI scan *(the preoperative*

*MRI scan can be used in patients who underwent biopsy only)* and will include any T2 abnormality

suspected of containing tumor plus a 2 cm margin *(to block edge).* If the tumor has been completely

resected, the target volume will be the surgical defect and any T2 abnormality surrounding the surgical

defect plus a 2 cm margin *(to block edge).* **There will be no boost volume.** The margin may be reduced

to a 1 cm margin *(to block edge)* around critical structures *(See Section 6.4)* and/or natural barriers to

tumor growth *(e.g. skull and tentorium).*

**6.3 Dose, Schedule, Dosimetry, and Compliance Criteria**

Treatment will be given in 1.8 Gy fractions *(to isocenter),* 1 fraction per day, 5 days per week and must

begin within four weeks after randomization. The total dose will be 54 Gy in 30 fractions over

approximately 6 weeks. The target volume must receive 95-105% of the prescribed total dose to be per

protocol *(encompassed by the 51.3 to 56.7 Gy isodose line)*.

If the target volume receives 90-94% or 106-110% of the prescribed total dose, an acceptable variation will

be assigned.

If the target volume receives < 90% or >110% of the prescribed total dose, an unacceptable deviation will

be assigned.

Other variances from protocol radiotherapy will be assigned as follows:

≤ 5% variation from protocol specifications-per protocol;

6-10% - acceptable variation;

>10% - unacceptable deviation.

The isodose distribution in the transverse *(axial)* plane through the geometric center of the target volume

must be submitted to RTOG for review.

**6.4 Critical Structures**

Every attempt should be made to shield the globes *(including lenses and retinae)* from any direct radiation

beams. A portion of one globe may receive ≤ 10 Gy. The pituitary gland, optic chiasm, or brainstem

*(medulla, pons, midbrain)* may not receive > 105% *(56.7 Gy)* of the prescribed total dose of 54 Gy.

Uninvolved contralateral normal brain may not receive > 36 Gy.

9802: 10 yr OS 40% 🡪 60%. MS 7.8 to 13.3 years. PFS 21%--> 51% (XRT + PCV)

PCV = procarbazine, lomustin/CCNU, vincristine

Oligodendroglioma and xrt+pcv favorable prognostic factors.

<40 yo and STR or >40yo + any

Grade 2 astrocytoma, oligodendroglioma, oligoastrycytoma

Dose: 54Gy in 1.8Gy fractions

Chemo after radiation. PCV starts one month after radiation.

Margins: postop mri brain scan. (can look at preop mri brain scan). T2 weighted MRI and any surgical defect. +2cm margin tumor edge to block edge (before IMRT needing Penumbra).

Soltys Stanford margin: 1.5cm to 54Gy

9802: 10 yr OS 40% 🡪 60%. MS 7.8 to 13.3 years. PFS 21%--> 51% (XRT + PCV)

PCV = procarbazine, lomustin/CCNU, vincristine

Oligodendroglioma and xrt+pcv favorable prognostic factors.

<40 yo and STR or >40yo + any

Grade 2 astrocytoma, oligodendroglioma, oligoastrycytoma

Dose: 54Gy in 1.8Gy fractions

Chemo after radiation. PCV starts one month after radiation.

Margins: postop mri brain scan. (can look at preop mri brain scan). T2 weighted MRI and any surgical defect. +2cm margin tumor edge to block edge (before IMRT needing Penumbra).

Soltys Stanford margin: 1.5cm to 54Gy

7.2 Radiotherapy for High Risk **Low Grade Glioma** (for radiotherapy for Anaplastic Glioma please see Section 7.1)

Radiation therapy will use the same regimen in Arms A and B.

If planning to utilize IMRT, please also refer to Appendix XI ‘ATC Guidelines for the Use of IMRT (including Intra-Thoracic Treatments)’. Patients must not receive proton radiotherapy or stereotactic radiosurgery.

7.21 Radiation Energy

Minimum photon energy of 4MV with multiple ports designed and verified by simulation. If IMRT is utilized, 6 MV is preferred. Minimum SSD or SAD of 80 cm.

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7.22 Treatment Volumes

7.221 Gross Tumor Volumes (GTV)

A postoperative MRI must be used for tumor localization, with the exception of 1) patient in whom MRI is contraindicated (e.g., pacemaker, claustrophobia, etc.) in which case a CT scan can be used, and 2) patients who underwent biopsy only; in which case the preoperative MRI scan can be used.

For purposes of the protocol, the GTV1 will be the so-called “edema volume” which is best visualized on the FLAIR or T2-weighted MR images. If tumor enhancement is present this should be included in the GTV1 as well. The GTV1 should also include the surgical resection cavity and any FLAIR or T2 abnormalities beyond the edges of the cavity. In the case of a gross total resection without any residual FLAIR/T2 abnormalities, then the surgical cavity will be considered the GTV1.

In cases where a partial or complete lobectomy has been performed, the region anterior to the edge of the resection (i.e., where no brain tissue is present) does not necessarily need to be included in the GTV1 (or the CTV1). For example, if a patient has an anterior temporal lobectomy, the anterior middle cranial fossa does not need to be included in the tumor volume. In this situation, the GTV1 should encompass the resection margin and any FLAIR to T2-weighted abnormalities and areas of tumor enhancement.

7.222 Clinical Target Volume (CTV)

The CTV1 is the GTV1 plus a margin of 1.0 cm in all directions. However, the CTV1 must not extend outside the brain. The CTV1 may also be modified to meet critical dose constraints (e.g., optic nerves) but should never be less than the GTV1.

In cases where a partial or complete lobectomy has been performed, the region anterior to the edge of the resection (i.e., where no brain tissue is present) does not necessarily need to be included in the CTV1. For example, if a patient has an anterior temporal lobectomy, the anterior middle cranial fossa does not need to be included in the tumor volume. In this situation, the CTV1 should be an expansion of the GTV1 in all directions, but not into the resection cavity.

7.223 Planning Target Volume (PTV)

The PTV1 is the CTV1 plus a 3 to 5 mm margin in all directions to account for daily setup variation and patient movement, but not beam penumbra or buildup. Generally another 5-7 mm is added to block edge in 3D planning to account for penumbra.

7.224 Internal Margin (IM) and Set-Up Margin (SM): There will be no IM or SM.

7.23 Prescription Isodose

The prescription isodose (i.e. the isodose that is 100% of the prescription dose) shall be the isodose surface (i.e. curve) that encompasses 95% of the PTV. In

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addition, the goal of the treatment plan is to encompass the entire PTV within the 95% isodose surface.

7.24 Tissue Heterogeneity

Calculations are required for IMRT and strongly recommended for 3D treatment planning to take into account the effect of tissue heterogeneities whenever CT-based planning is used. See Appendix XI for the ATC Guidelines for IMRT.

7.25 Total Dose

7.151 3D or IMRT Total Dose

The dose to the prescription isodose for the PTV1 (derived from the GTV1 – see above) will be 5040 cGy in 28 daily fractions of 180 cGy each. The dose will be delivered to the treatment volumes as previously described.

7.26 Dose Uniformity

The entire PTV1 shall be encompassed within the 95% isodose surface as evaluated by dose volume histogram. Please note it is preferable that 95% or more of the PTV1 receives the prescribed dose.

7.27 Time Considerations

Patients will receive one treatment per day, five days per week (Monday through Friday). All fields will be treated each day. At least two fractions must be given during the first week of treatment.

7.271 Interruptions

No special considerations need to be made for treatment delays of 1 week or less. Treatment may be given on weekends to make up for treatment interruptions. If treatment is delayed more than 1 week, notify the study chair.

7.28 Simulation

Simulation will be performed using either a conventional CT or MRI simulator.

7.281 Patient Position and Immobilization

The patient shall be treated in the supine or other appropriate position, depending on the location of the lesion. A head-holding device that is transparent to x-rays (thermoplast masks, bit-block, etc.) must be used to ensure adequate immobilization during therapy of reproducible treatment setups.

7.29a Organs at Risk (OAR)

When possible, without shielding GTV/CTV/PTV, no more than 0.03 cc of each of the following OAR should receive more than the following doses: brainstem 5500 cGy, optic nerves and optic chiasm 5400 cGy, retina 4500 cGy, cervical spinal cord 5000 cGy, and lens 1000 cGy. These constraints should have a higher priority than the target volumes.

Planning organ at risk volumes (PRVs) are recommended such that the spinal cord should have 3-dimensional expansion by 5 mm while the optic nerves, optic chiasm, and brainstem should have a 3 dimensional expansion by at least 1 mm.

The dose constraints to the PRVs will be the same as for their respective OARs as outlined above.

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Lower priority (lower priority than PTV coverage) include: Parotids (entire volume) ≤ 10 Gy, oral cavity/lips/nasal cavity mean dose 20 Gy and < 1% > 40 Gy; inner/middle ear mean dose 30 Gy and < 1% > 50 Gy; lens as low as reasonably possible. Typically 100% of the parotids should receive < 10 Gy, but tumor coverage is of higher priority in cases where this dose will exceed 10 Gy. If possible, no more than 1% or 1 cc of the contralateral uninvolved brain should receive more than 3000 cGy. Also, no more than 1% or 1 cc of unspecified tissue outside of the PTV is to receive > 110% of the prescribed dose.

7.29b Dose Calculation and Reporting

Isodose distributions must be submitted for the treatment plan. IMRT plans must be submitted electronically to IROC Rhode Island QA Center (QARC). 3D CRT plans should be submitted to IROC Rhode Island but may be submitted in hard copy if digital submission is not possible. See IROC Rhode Island web page (http:// http://irocri.qarc.org) for instructions on establishing an account with IROC Rhode Island and submitting data. The instruction can be found by clicking on the IROC Rhode Island link from the website. The prescription isodose and the outlines of the planning target volume and critical organs must be shown. Isodose values must be clearly labeled. Isodose distributions in the axial, sagittal and coronal planes, which include the isocenter of the planning target volume (PTV), must be submitted. For 3D/IMRT treatment plans in which the sagittal and coronal planes are not available, a minimum of five axial distributions must be submitted (central axis, two superior, and two inferior planes).For questions regarding digital data submission, please contact IROC Rhode Island at irocri.qarc.org or 401-753-7600.

Please refer to Section 18 Records and Data Collection Procedures for further instructions regarding submission of materials for radiation therapy quality assurance.

7.29c Dose Volume Histograms

Dose volume histograms must include GTVs, CTVs, PTVs, and OARs as noted above. A DVH in absolute dose must also be submitted for so called “unspecified tissue,” i.e., tissue contained within the skin, but not included with the GTV, CTV, PTV, or OAR.

7.29d IMRT Plan Verification

If IMRT is used, the monitor units generated by the IMRT planning system must be independently checked prior to the patient’s first treatment. Measurements in a QA phantom can suffice for a check as long as the plan’s fluence distribution can be re-computed for a phantom geometry.

7.29e Quality Control and Definitions of Deviations

These will be done according to the guidelines in Appendix X. All plans and associated materials as per NCCTG standard will be reviewed by 2 radiation oncologists and the IROC.

7.29f Verification of Treatment Set-Up

Port films of each field will be obtained and compared with initial simulation films at least weekly. Alternatively, after initial ports are taken of all fields (excluding vertex), an orthogonal pair of reference ports may be taken on a weekly basis. For

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IMRT, orthogonal pair of reference films is sufficient for the initial and subsequent ports.

Questions regarding the radiotherapy section of this protocol should be directed to the Radiation Oncology Study Co-Chair Dr. Paul Brown, M.D. at the contact information listed on page 2 of the protocol.

The details of ct simulation were explained in detail to the patient including use of mask, bolus, body positioning.

Acute and late Side effects include but not limited to: hair loss, fatigue, scalp soreness, scalp erythema, nausea, vomiting, headaches, seizures, weakness, ear canal reactions, hearing impairment, dry mouth, altered taste, skin reaction, mucositis (if nasopharynx in treatment field more risk of mucositis and loss of taste), loss of short term memory. Other late side effects include but not limited to: radiation necrosis, neurocognitive disorder, risk of memory loss, personality changes, weakness, leukoencephalopathy, infections, endocrine dysfunction, radiation induced cancers, permanent hearing loss, permanent vision loss, cataracts.