Radiotherapy Protocols

RADICAL CRANIAL RADIOTHERAPY

Prepared by C Blesing, N Warner, T Foord, S De Silva-Minor, C Charlton and H Eldeeb and applies across the Thames Valley Cancer Network. *This updated includes contribution from D Cutter and R Davis*

For Paediatric patients: the appropriate *study protocol or CCLG (Childrens Cancer and Leukaemia Group) guideline or guidance from appropriate CCLG lead (which should be documented in the patient’s record) must always be used and given priority over this document. Please also use the department paediatric protocol in conjunction with this document (RTProt/Paed).*

Current paediatric protocols/guidelines are usually available digitally and can be found on the OUH Trust *intranet: Paediatric Haematology and Oncology > treatment protocols*. In the absence of a Consultant Paediatric Radiotherapist please contact the Paediatric Oncology Consultant of the Week for advice *via Kamran’s ward (01865 (2)34068/9)*

For patients requiring ‘whole CNS treatment’, this is covered in **CD-L3-002**.

For rare tumours please see the BNOS /National Cancer Action Team [www.bnos.org.uk](http://www.bnos.org.uk)

Rare Brain and CNS Tumours. Guidelines on the diagnosis and management of:

1. Primary CNS and intra-ocular Lymphoma (PCNSL)
2. Optic Pathway Glioma (OPG)
3. Adult Pineal area tumours
4. Adult PNET

**INDICATIONS**

**Low Grade Glioma.**

- Following evidence of disease progression on imaging
- Persistent symptoms difficult to control medically (*e.g.* seizures)
- Disease affecting a critical site (*e.g.* optic chiasm) at outset.

**High Grade Glioma**

(*Glioblastoma, Anaplastic Astrocytoma, Anaplastic Oligodendroglioma, Anaplastic Ependymoma*)

- Post op RT should be considered for all patients.
- Radical course for age <70 PS 0-2
- Consider Temozolomide +RT for patients with GBM, PS ≤1, Age ≤ 70
- Consider Temozolomide alone for GBM age >70 meth MGMT positive
- Consider hypofractionated RT (34Gy in 10#) GBM >70 meth MGMT negative, PS 0-1
- Consider adjuvant post RT PCV x 6 chemotherapy for patients with anaplastic oligodendroglioma with1p19qloss
- Consider BR14 trial for Grade 3 anaplastic astrocytoma or anaplastic oligodendroglioma without 1p19q loss

*See Palliative Brain guidelines for poor prognosis Glioma patients* (*i.e.* all others not included above).

**Meningioma**

- For incompletely resected disease in critical sites, or recurrent Grade 1 or Grade 2 Meningioma usually following second operation.
Consider RT for all Grade 3 Meningioma (following complete/partial or no resection)

**Pituitary Adenoma**
- Post op residual extra-sellar disease or continued hormone secretion despite surgery / medical therapy.
- Recurrent disease in patients who initially had surgery alone
- Stereotactic radiotherapy / radiosurgery can be considered for relapse >3mm from optic chiasm in patients who have undergone surgery and external beam RT (45Gy)

**Craniopharyngioma**
- Following partial resection or recurrence

**Pineal Tumours**

*Malignant Non-Germinomatous Germ Cell Tumour – secreting (NGGCT)*
Localised, non metastatic MGNGCT following induction chemotherapy. (See BNOS guidelines)

**Primary CNS Lymphoma** (see [www.bnos.org.uk](http://www.bnos.org.uk) for national guidelines)
Combined modality post chemotherapy in selected younger patients with complete response
Residual disease resistant to methotrexate based chemotherapy
Recurrent disease
Elderly patients unfit for chemotherapy

(Avoid *combining chemo and* Radiotherapy in patients > 60 yrs due to high incidence of dementia)

**Cranial RT for A.L.L. (including prophylactic cranial radiotherapy)**
- Patients with CNS disease at presentation.
- Patients with an isolated CNS relapse on or off treatment who have not previously received radiotherapy.
- Testicular involvement at presentation.
- or
- Follow relevant clinical trial protocol.

If CSF+ disease, patient to receive Whole CNS treatment following **CD-L3-002**

**PRE-RADIOThERAPY INVESTIGATIONs**
- Pre and post op (where available) imaging (MRI or CT)
- FBC, Biochem all patients. Phenytoin levels in patients receiving this drug. NB Blood tests within 7 days of starting treatment for those receiving Temozolamide.
- Visual Fields within last 6 months for pituitary irradiation.
- Histological confirmation of diagnosis unless exceptional circumstances

**IMMOBILISATION / PATIENT POSITION**

**Radical Brain RT:**
Immobilisation shell: Patient position depends on site of lesion and fields being used.

- The majority of patients should be positioned supine with neck fully flexed. Use an angled support for temporo-parietal lesions if possible.
- Occasionally it may be appropriate to use a prone shell for posterior lesions.
CT planning
- Use image fusion with MRI / diagnostic CT to enhance GTV and OAR definition
- Use IV contrast in absence of contraindication at clinician request (particularly if no fusion available).

Treatment modality and energy
6 MV photons.

Shielding
Shield optic chiasm, lenses and field outside PTV.

Normal Tissue tolerance (maximum) doses
See QUANTEC papers Int. J. Radiation Oncology Biol. Phys., 2010 Vol. 76, No. 3, Supplement,

<table>
<thead>
<tr>
<th>Normal Tissue</th>
<th>Dmax</th>
<th>Radiation induced optic neuropathy (RION)</th>
<th>RION incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic chiasm</td>
<td>&lt;55 Gy (&lt;=2Gy#)</td>
<td>negligible</td>
<td>3-7%</td>
</tr>
<tr>
<td></td>
<td>55–60 Gy (&lt;=2Gy#)</td>
<td>RION</td>
<td>&gt;7–20%</td>
</tr>
<tr>
<td></td>
<td>&gt;60Gy (&lt;=2Gy#)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbit</td>
<td>Dmax 50Gy in 2Gy #</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lens</td>
<td>Dmax 6Gy (2Gy #)</td>
<td>&lt;1% risk cataract,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10Gy (2Gy#)</td>
<td>50% risk of cataract</td>
<td></td>
</tr>
<tr>
<td>Brain stem</td>
<td>Dmax 54Gy (2Gy #) to entire brain stem.</td>
<td>Risk &lt;5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>aV59 &lt;=10cm³</td>
<td>(absolute volume receiving 59Gy &lt;= 10 cm³)</td>
<td>risk &lt;5%</td>
</tr>
</tbody>
</table>

Outline – *see RTProt/ CNS Contouring for details*
- Orbit
- lens
- Optic nerve, optic chiasm and brainstem if these are in/near treatment beams.
- *Add a margin of at least 0.2cm to give the Planning Organ at Risk Volume (PRV) (OUH data)*

Usual field arrangement
- Preferably at least three fields for radical brain treatment
- Reduce irradiation of contra-lateral hemisphere if possible. (Aim for <60% of prescribed dose)
- A three-field + beam arrangement reduces permanent hair loss.
- Pituitary can use 4 field arrangement using vertex field.

Overall treatment time – category 2
Patients should be scheduled to start their radiotherapy on a Tuesday so that this ties in with the weekly clinic review and clinicians giving the patient the Temozolamide prescription if appropriate.

Verification
- Refer to the departmental verification imaging policies (see OCC-VI-L2-001 and OCC-VI-L3-001)
- Eye TLDs are not routinely required but may be requested
**Review on treatment**

- On treatment review by clinician following *routine* review schedule or as per external protocol
- Weekly FBC and U+E and LFT (±/- phenytoin levels if requested) for those receiving concomitant chemotherapy.
- Monitor steroid dose closely during and following radiotherapy; lower slowly if no symptoms of raised intra-cranial pressure.

**Radical Cranial Radiotherapy Prescription / prescription point and target definition:**

Prescription doses for guidance only;

For Adults, prioritise to relevant NCRI protocol if in existence

For Paediatrics, see statement on page 1 re using CCLG and local paediatric protocols.

<table>
<thead>
<tr>
<th>Malignant Glioma</th>
<th>59.4Gy in 33# (1.8Gy #) or 60Gy in 30 (2Gy #) daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Glioblastoma, Anaplastic Astrocytoma, Anaplastic Oligodendroglioma)</td>
<td>(33# if Grade 3 or chiasm included in PTV) to ICRU reference point (100%)</td>
</tr>
<tr>
<td>Meningioma Grade 3</td>
<td>● GTV = post op residual tumour and resection cavity (consider pre op tumour volume).</td>
</tr>
<tr>
<td></td>
<td>● CTV = GTV + 2.0cm including all T2 abnormality /oedema or to anatomical boundary(extend across mid line only if corpus callosum is involved),</td>
</tr>
<tr>
<td></td>
<td>● PTV = CTV + 0.5 cm</td>
</tr>
<tr>
<td><strong>Brain stem:</strong></td>
<td>54Gy in 30 (1.8Gy)#</td>
</tr>
<tr>
<td>Special sites:</td>
<td></td>
</tr>
<tr>
<td>Low Grade Glioma, Localised Ependymoma (low and high grade anaplastic) Meningioma Grade 1 or 2</td>
<td>54Gy in 30 # (daily 1.8Gy fractions) to ICRU reference point (100%)</td>
</tr>
<tr>
<td></td>
<td>● GTV = POST-OP tumour volume on T2 for glioma or T1+ contrast for meningioma (consider post and pre op imaging as well)</td>
</tr>
<tr>
<td></td>
<td>● CTV = GTV + 1.0cm or to anatomical boundary (extend across mid line only if corpus callosum is involved),</td>
</tr>
<tr>
<td></td>
<td>● PTV = CTV + 0.5cm</td>
</tr>
<tr>
<td><strong>Brain stem:</strong></td>
<td>50 - 54Gy in 28 - 30 # (daily 1.8Gy fractions).</td>
</tr>
<tr>
<td><strong>Optic glioma:</strong></td>
<td>54Gy in 30# (daily 1.8Gy fractions).</td>
</tr>
<tr>
<td>Special sites:</td>
<td></td>
</tr>
<tr>
<td>Pituitary Adenoma</td>
<td>45Gy in 25 # (daily 1.8Gy fractions) to ICRU reference point or (50Gy/ in 30# (daily 1.67 Gy fractions) for large Macroadenomas)</td>
</tr>
<tr>
<td></td>
<td>● GTV = POST-OP tumour volume (consider post and pre-op tumour volume imaging as well).</td>
</tr>
<tr>
<td></td>
<td>● CTV = GTV + whole cavernous sinus if involved</td>
</tr>
<tr>
<td></td>
<td>● PTV = CTV + 0.5cm</td>
</tr>
<tr>
<td>Craniopharyngioma</td>
<td>50Gy in 30# (daily 1.67 Gy fractions) to ICRU reference point (54Gy/ in 33# (daily 1.64 Gy fractions) for selected large cases)</td>
</tr>
<tr>
<td></td>
<td>● GTV = POST-OP tumour volume (consider post and pre op tumour volume imaging as well).</td>
</tr>
<tr>
<td></td>
<td>● CTV = GTV</td>
</tr>
<tr>
<td></td>
<td>● PTV = CTV + 0.5cm</td>
</tr>
<tr>
<td>Malignant Non- Germinomatous Germ cell tumour (Secreting NGGCT)</td>
<td>54 Gy in 30 fractions (1.8Gy)</td>
</tr>
<tr>
<td>Pineocytoma and Intermediate differentiation pineal tumour</td>
<td>50 – 54Gy in 30 fractions (1.6 – 1.8Gy)</td>
</tr>
<tr>
<td></td>
<td>● GTV = visible residual tumour and/or tumour bed</td>
</tr>
<tr>
<td></td>
<td>● CTV = GTV + 1cm</td>
</tr>
<tr>
<td></td>
<td>● PTV = CTV + 0.5cm</td>
</tr>
<tr>
<td>Condition</td>
<td>Treatment Details</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Primary CNS Lymphoma</strong></td>
<td></td>
</tr>
<tr>
<td>If &lt;60 yrs</td>
<td>45 Gy / 25 (daily 1.8Gy fractions)</td>
</tr>
<tr>
<td>If &gt;60 yrs</td>
<td>30.6 Gy/17 (daily 1.8Gy fractions)</td>
</tr>
<tr>
<td></td>
<td>CTV = Whole Brain (including optic nerves)</td>
</tr>
<tr>
<td></td>
<td>PTV = CTV + 0.5cm</td>
</tr>
<tr>
<td><strong>Acute Lymphoblastic Leukaemia (ALL)</strong></td>
<td></td>
</tr>
<tr>
<td>(including prophylactic cranial irradiation)</td>
<td>24Gy /12# (daily 2Gy fractions)</td>
</tr>
<tr>
<td></td>
<td>CTV = Whole Brain (including optic nerves)</td>
</tr>
<tr>
<td></td>
<td>PTV = CTV + 0.5cm</td>
</tr>
</tbody>
</table>
PALLIATIVE CRANIAL RADIOTHERAPY

INDICATIONS
- High grade Glioma not suitable for radical RT
- Age > 70 methylated MGMT negative.
- Poor prognosis patients (consider age, PS and neurological deficit).
- Brain metastases (biopsy proven or known primary tumour).
- Primary CNS Lymphoma not suitable for radical RT.
- Other primary brain tumours not suitable for radical RT.
- Prophylactic cranial RT (PCI) for Small cell lung cancer (Both extensive and limited stage disease, performance status 0-2, with response to chemotherapy)

PRE-RADIOThERAPY INVESTIGATIONS
- If isolated metastases (1, 2 or occasionally 3) on MRI and NO progressive systemic disease, consider referral for neurosurgical resection or stereotactic radiotherapy. Therefore investigate as appropriate.

IMMOBILISATION / PATIENT POSITION
- Supine, with Thermoplastic immobilisation shell

CT planning
- Virtual CT simulation when part brain is being irradiated.
- Consider conventional simulation for whole brain RT.

Treatment modality and energy
6MV Photons

Target definition
- **High Grade Glioma**
  GTV = contrast enhancing tumour from pre-op imaging including T2 abnormality/oedema
  Field edge = GTV + 3.0cm

- **Brain metastases, CNS Lymphoma, and Prophylactic Cranial Irradiation for SCLC**
  CTV = whole Brain
  Field Margin = CTV + 1.0cm (include scalp in margin)

Normal Tissues to be outlined
None

Usual field arrangement
Whole Brain or part brain – opposed fields.
*CT planned volume focal irradiation for the higher palliative dose 34 Gy in 10 fractions.*
Palliative Cranial Radiotherapy Prescription / prescription point / critical organ dose limits

High Grade Glioma
34 Gy in 10# (3.4 Gy per fraction) over 2 weeks – CT planned volume (methylation MGMT negative and PS 0,1).
30Gy in 6# (5Gy per fraction) over 2 weeks to 100% (all ages, PS 2-3)

Primary CNS Lymphoma plus other primary brain tumours not suitable for radical RT
30.6Gy in 17# (1.8Gy fractions daily) or
30Gy in 10# (3Gy fractions daily) or
20Gy in 5# (4Gy fractions daily) to 100%

Prophylactic Cranial Irradiation for Small Cell Lung Cancer
Refer to Small Cell Lung Cancer protocol (RTProt/ Bro SCLC) for details.

Brain metastases

<table>
<thead>
<tr>
<th>RTOG Recursive Partitioning Analysis (RPA) for brain metastases</th>
<th>Median Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I KPS &gt;=70, &lt;65 years, controlled primary, no extra-cranial metastases.</td>
<td>7.1 months.</td>
</tr>
<tr>
<td>Class II Neither I nor III</td>
<td>4.2 months</td>
</tr>
<tr>
<td>Class III KPS &lt;70.</td>
<td>2.3 months</td>
</tr>
</tbody>
</table>

Good prognosis patients:
Following resection of limited brain metastases or stereotactic radiosurgery with no evidence of progressive systemic disease RPA class 1 and some class II.
Following resection of 1 to 3 isolated brain metastases, there is no evidence of survival benefit (median survival 10 months) from adjuvant cranial RT, however there is a delay in neurological progression of 1.2 months (from 3.4 to 4.6 months) (EORTC 22952 Kocher 2011)

If radiotherapy is given, Whole brain Radiotherapy (WBRT) 30Gy in 10 # (daily 3Gy fractions) mid plane dose + conformal Boost 12-15Gy/5# (daily 2.4Gy to 3Gy fractions)

Poor prognosis patients: (all other patients). All RPA class III and some class II.
Whole brain radiotherapy may have a role to play dependant on performance status. Dose 20 Gy in 5 fractions to mid plane if treated.

Overall treatment time – category 3

Verification
Refer to the departmental verification imaging policies (see OCC-VI-L2-001 and OCC-VI-L3-001)

Review on treatment
- On treatment review by clinician following routine review schedule or as per external protocol
LINKED DOCUMENTATION

CD-L3-002  Whole CNS Combined Protocol
OCC-CL-L2-001  Justification for Exposures Related to Therapeutic Radiation
OCC-CL-L2-003  Patient consent
ICRU 50
ICRU 62
OCC-EB-L4-004  Radical Brain Radiotherapy Treatment Delivery Competency
OCC-MR-L2-001  Mould Room Process
OCC-PP-L2-001  Planning Management and Responsibilities
OCC-PP-L2-002  Flow of Treatment Planning Information
OCC-PT-L2-001  Planning of External Beam radiotherapy – CT Scanner
OCC-PT-L2-002  Planning Radiotherapy – Acuity Simulator
OCC-PT-L3-001  Palliative Treatment Planning
OCC-PT-L4-007c  Head and Neck/ Brain Set-Up Information – S frame and Laminate board
OCC-PT-L4-006  Radical Planning Scan
OCC-RT-L2-001  Delivery of External Beam Radiotherapy
OCC-RT-L2-003  Use of In-Vivo Dosimetry
OCC-RT-L3-019  Patient Identification Procedure
OCC-TLD-L3-010  TLD Dosimetry, instructions for radiographers
OCC-VI-L2-001  Operator Led, Practitioner Directed Verification Imaging
OCC-VI-L3-001  Verification Imaging Tolerances and Frequency of Imaging
Pregnancy Policy
RT 4.4  Radiotherapy Planning Request form

RTProt/ CNS Contouring  Normal Tissue Contouring for CNS Tumours
RTProt/ Paed  Paediatric Radiotherapy Excluding Whole CNS