Thames Valley and Wessex Radiotherapy Operational Delivery Network (ODN)

Radiotherapy Protocols

Supine Whole Central Nervous System (CNS)

This document is the standardised Thames Valley and Wessex Radiotherapy Network Supine Whole Central Nervous System treatment protocol developed collaboratively by the ODN Neurological Cancers Protocol Working Group:

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Document History

Date of Issue	Version Number	Date Approved	Responsible for Change	Nature of Change	Ratification/ Approval
09/03/22	V0.1 (draft)	18/03/22	The Neuro Working Group	The original OUH protocol adapted	
07/04/22	V 1.0 (final)		The Neuro Working Group		Thames Valley and Wessex RT NOG
11/10/23	V2.0	11/10/23	The Neuro Working Group	Protocol review and update	Thames Valley and Wessex RT NOG

Contents

1. Primary Objective and Scope

To summarise the External Beam Radiotherapy treatment protocols for the whole central nervous system (whole CNS) for use in Radiotherapy Centres in the Thames Valley and Wessex Radiotherapy Network.

2. Clinical Requirements

N.B. for paediatric patients

- The appropriate study protocol or CCLG (Children's Cancer and Leukaemia Group) guideline or guidance from appropriate CCLG lead (which should be documented in the patient's record on EPR) must always be used and given priority over this document. A copy of the relevant sections will be kept in the patients' record.
- For all patients under 27 years, check current proton referral criteria with NHSE or consider proton referral

2.1. Indications

- Medulloblastoma, ependymoblastoma, pineoblastoma (e.g., sub types previously called PNET)
- Metastatic ependymoma
- Intracranial germ cell tumour (refer to CCLG for full details)
- CSF relapsed leukaemia (when indicated by relevant protocols)
- In adult cases of ALL, craniospinal irradiation is rarely used other than for individualised cases for palliation of relapsed patients with no other therapeutic options
- Metastatic choroid plexus tumour
- Rarely other metastatic primary CNS tumours

2.2. Pre-radiotherapy Investigation

- Pre- and post-operative MRI of brain and spine
- Cerebro Spinal Fluid (CSF) for cytology (before or more than 14 days after surgery) for medulloblastoma, ependymoma, germ cell and leukaemias
- FBC, U&E, LFT, pituitary baseline bloods, tumour markers αFP, βHCG (CSF and serum) for midline lesions which might be germ cell
- Referral to other teams eg. ophthalmology, audiology if appropriate
- Consider fertility ovarian preservation especially if chemo planned after RT. Further information can be found OUH: http://orh.oxnet.nhs.uk/PaedHaemOnc/Pages/OvarianCryopreservation.aspx

- UHS: HTTP://STAFFNET/OURTRUST/PEOPLEANDPLACES/DEPARTMENTS/DIVISIONC/WOMENANDNEWBORN/FERTILITY/FERTILITY-PRESERVATION.ASPX

3. Target Definition

PHASE 1

Brain

- **CTV = Whole brain including the cribriform plate**
  - Outline the whole brain and brain stem down to the bottom of the foramen magnum.
  - Ensure coverage of temporal fossa, cribriform plate and any meningocele (herniation of the meninges through a craniotomy scar).
  - Use bone and soft tissue windows to check all brain tissue is included.
- **PTV/Field edges (Conformal)**
  - Facial MLC shielding is used ensuring that the whole cranial fields provide adequate coverage of the whole brain CTV (field edge outside skull) and Phase II (boost) PTV. This must be checked when the plan is approved.
- **PTV = CTV + 0.5 cm (VMAT)**

Spine

- **CTV = Spinal cord and thecal sac**
  - Outline the whole spinal canal (to its bony limit), including the medial part of the intervertebral foramina (to cover circulating CSF), to the bottom of the thecal sac (usually at about S2, defined as 1cm below the end of the thecal sac on sagittal T1-weighted MRI with radiologist assistance if necessary).
- **PTV = Spine CTV + 0.5 - 1cm laterally and inferiorly (Conformal)**
  - No anterior, posterior or superior margin.
  - Ensure that the resultant width of the spine PTV is clinically appropriate. In sacrum, do not contour the separate nerve root exit foramen when it is anatomically distinct from the cauda equina canal.
  - Add inferior margin manually.
- **PTV = CTV + 0.5 - 1cm for VMAT (also for spinal boost)**

PHASE 2 BOOST

- Use MRI/CT fusion with pre- and post-operative imaging for target delineation (MRI T1 with contrast and T2).

Boost (in the absence of a CCLG/study protocol)

- **GTV** - includes all gross residual tumour and/or the walls of the resection cavity at the primary site, based on the initial imaging examination that defines the tissue initially involved with disease anatomically and the post-operative and pre-irradiation neuro-imaging examinations.
  The GTV should account for any anatomical shift or changes after surgery.
- **CTV = GTV + 0.5- 1 cm** – depending on tumour definition, constrained by bone or the tentorial interface where the disease is confined to the posterior fossa. Do not include meningocele.
  If there are concerns regarding the GTV definition (e.g., poor quality MRI), then consider 1.5cm margins. N.B. Consider ventricular spread in the boost as appropriate clinically

- **PTV = CTV + minimum of 0.5cm** in all directions (for both conformal and VMAT) and for Spine boost see above margins in spine section

4. Normal Tissue Dose Constraints

NORMAL TISSUES TO BE OUTLINED (including tolerance doses where appropriate)
See **RTProt/ CNS Contouring** for anatomical detail

Normal Tissue tolerance (maximum) doses: <2Gy/fraction
See QUANTEC papers Int. J. Radiation Oncology Biol. Phys., 2010 Vol. 76, No. 3, Supplement

For > 2Gy/ fraction hotspots >107% should be avoided in OARs.

Structure	Dose to 0.1cm³ (*$D_{0.03cc}$)		Mean dose
	Optimal	Mandatory	
Cord PRV	50 Gy	54 Gy	
Brainstem PRV	54 Gy	V54Gy < 10cc $D_{0.1cc}$ < 59 Gy	
Optic nerves/ chiasm PRV ($D_{0.03cc}$)		54 Gy	
Orbit PRV (Retina)	45 Gy	50 Gy	
PTV coverage should NOT be compromised to meet the constraints shown below:			
Lacrimal gland ($D_{0.03cc}$)	≤ 30Gy		
Pituitary	For information only		
Brain (D_{1cc})	-	60 Gy	
Lenses ($D_{0.03cc}$)	6 Gy	10 Gy	
Cochlea (ipsilateral)	-	-	45Gy Spare contralateral cochlea – keep mean dose below 10-25 Gy
Whole Parotid	-	-	< 24 Gy

Cerebellum, Hippocampus, Hypothalamus & Supratentorial brain	To document dose, if outlined	
Kidneys	V_{12} Gy < 55%	< 5% risk, for combined kidneys
	V_{20} Gy < 32%	< 5% risk, for combined kidneys
	V_{23} Gy < 30%	< 5% risk, for combined kidneys
	V_{28} Gy < 20%	< 5% risk, for combined kidneys
Heart	*Minimise mean heart dose, V_{15} and V_{30} as much as practically achievable, ideally these should be < 10 Gy, < 25% and < 10%*	
Ovaries (if possible) or Testes (as appropriate)	*Mean dose < 5 Gy* *Maximum dose of 10 Gy to any part of the volume outside PTV* *If inside PTV discuss individual case with Consultant and consider fertility preservation in pre-menopausal women*	
Thyroid	*D_{100} < 45 Gy. V30≤62.5% predicts a low risk of hypothyroidism*	Lifelong monitoring will be required
Breast buds	*Minimise mean dose (aim <2 Gy) and V_4, particularly in women < 36 years*	
Spleen	*Mean < 10 Gy*	
Lungs	*V_{5Gy} < 65%, mean < 15 Gy and V_{20Gy} < 30%*	
Oesophagus	*Mean dose < 34 Gy, V_{35} < 50%*	
Liver	Mean dose < 32 Gy; V_{40} of 30-35%	

If the mean splenic dose is >10 Gy the patient should be considered at high risk for functional hypo-splenism and managed based on national guidelines from the British Committee for Standards in Haematology.
This should include pneumococcal, haemophilus influenza type B conjugate vaccine, meningococcal conjugate vaccine at least 2 weeks prior to starting radiotherapy. In addition, prophylactic antibiotics should be offered and started when radiotherapy starts and given a supply of emergency antibiotics.

5. PRESCRIPTION (consistent with external protocol for disease site)

ADULT PATIENTS (18+)

Medulloblastoma **Metastatic Ependymoma** **Ependymoblastoma** **Pineoblastoma** **Choroid Plexus Tumour** **Metastatic other primary CNS tumours.**	**If low risk / non metastatic:** Brain and spinal theca 35 Gy in 21#s (1.67 Gy #s) x 5/wk Boost to primary site 20 Gy in 12#s (1.67 Gy #s) x 5/wk (usually posterior fossa) **If metastatic:** Boost to spinal mets. 10-15 Gy in 6-9#s (1.67 Gy #s) x 5/wk
Intracranial Germinoma (metastatic – see cranial protocol for localised disease)	Brain and spinal theca 24 Gy in 15#s (1.6 Gy #s) x 5/wk Boost to tumour site 16 Gy in 10#s (1.6 Gy #s) x 5/wk
Metastatic Secreting Germ Cell tumour (Consider ventricular spread in the boost)	Brain and spinal theca 30 Gy in 20#s (1.5 Gy #s) x 5/wk Boost to tumour site 24 Gy in 15#s (1.6 Gy #s) x 5/wk Boost to spinal mets. 16 Gy in 10# (1.6 Gy #s) x 5/wk
Acute Lymphoblastic Leukaemia (ALL) with CSF positive disease	Brain 24 Gy in 12#s x 5/wk spinal theca 12 Gy in 6#s x 5/wk (or as per specific protocol)

Overall treatment time

- Category 1 for paediatric malignancy, adult medulloblastoma and adult germ cell tumours – refer to your local protocol
- Daily fractions, weekdays

CHEMOTHERAPY-CONCURRENT, PRE AND POST RADIOTHERAPY TREATMENT

Paediatric Patients

- Refer to the relevant study protocol or CCLG guideline for details of concurrent, pre- and post-RT chemotherapy given to paediatric patients

Adult Patients

Medulloblastoma, ependymoblastoma, pineoblastoma (e.g., sub types previously called PNET)

- Particularly for TYA spectrum, adjuvant chemotherapy is recommended.
- Adjuvant chemotherapy starts 6 weeks following the completion of radiotherapy provided blood count recovery

Malignant non-Germinomatous Germ cell tumour (secreting GCTs)

- Initial treatment: 4 courses of PEI (see below) should be given at 21-day intervals, subject to count recovery
- Surgery should be considered for residual tumour after chemotherapy, followed then by radiotherapy (Cranio-Spinal Irradiation for metastatic, and localised 54Gy in 30# for primary only)

Malignant Glioma

- Concurrent temozolomide

Anti-emetics

Should be provided during the whole CNS phase

- 5-HT3 antagonists are usually used, or alternative
- Anti-emetic guidelines for the prophylaxis of chemotherapy and radiotherapy induced nausea and vomiting in adults is available form the OUH shared point: Cancer - TVCN antiemetic guideline v8.4 November 2021.pdf - All Documents (sharepoint.com)

6. On-Treatment Review

Patient weight:

- Should be recorded at new patient consultation at CT planning scan
- Record weekly whilst on treatment where possible
- If > 5% weight change from baseline (at CT) consider further verification of treatment accuracy and dietetic input.

7. Post-treatment

- Yearly pituitary function to be checked and referral made to endocrinology as appropriate.