Thames Valley and Wessex Radiotherapy Network (RTN_

Radiotherapy Protocols

ADULT Primary CNS Tumours (including benign)

This document is the standardised Thames Valley and Wessex Radiotherapy Network Adult Primary CNS Tumours (including benign) treatment protocol developed collaboratively by the RTN 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
18.08.2021	V 0.1 (1st draft)		The Neuro Working Group	Aligning existing local protocols and existing published evidence	
20.10.2021	V 0.2 (2nd draft)		The Neuro Working Group		
07/02/22	V 0.3 (3rd draft)		The Neuro Working Group	Changes made in line with the latest published evidence	
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01.10.2023	V2.0		The Neuro Working Group	Updated in line with the latest clinical evidence	
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Contents

1. Primary Objective and Scope

To summarise the planning and treatment of adult patients receiving external beam radiotherapy treatment for primary central nervous system (CNS) tumours (including benign) for use in Radiotherapy Centres in the Thames Valley and Wessex Radiotherapy Network.

2. Indications

Exclusion Criteria

1. Primary CNS Lymphoma refer to Lymphoma protocol.
2. Consider proton therapy for all patients <25 years old and chordoma/chondrosarcoma for all age groups as per NHSE proton guidelines: https://www.england.nhs.uk/commissioning/spec-services/highly-spec-services/pbt/. Consider referral to PBT services for other patients on a case by case basis.

Inclusion Criteria

Clinical Indication (including treatment criteria)	Grade / stage	Genetics	Dose (Gy)	Fractionation	Radiotherapy technique	Chemotherapy
GBM/Astrocytoma (≤ 70 y.o. PS ≤ 2) (nb also if post op haemorrhage caused PS3+)	**4**		60 (55 if concern re very large volume e.g 2/3 of brain volume or organ at risk tolerances)	30	VMAT/IMRT	Concurrent and Adjuvant Temozolomide x 6 (consider up to 12 only if residual responding disease)
GBM/Astrocytoma (≥ 70 y.o. PS ≤ 2 or no biopsy)	**4**	Meth MGMT Negative or no biopsy	40	15	VMAT/IMRT	No

GBM/Astrocytoma (≥ 70 y.o. PS ≤ 2)	**4**	Meth MGMT positive	40	15	VMAT/IMRT	Concurrent and Adjuvant Temozolomide x 6-12
GBM/Astrocytoma (PS 3+ or no biopsy)	**4**	Meth MGMT negative or no biopsy	34	10	Conformal or VMAT/IMRT	No

GBM (PS 3+)	**4**	Any or no biopsy	30	6 (over 2 weeks)	Conformal or VMAT/IMRT	no
Clinical Indication (including treatment criteria)	**Grade / stage**	**Genetics**	**Dose (Gy)**	**Fractionation**	**Radiotherapy technique**	**Chemotherapy**
Oligodendroglioma	**3**	1p19q co-deletion	59.4 (54-55/30 if concern re very large volume e.g 2/3 of brain volume or organ at risk tolerances)	33	VMAT/IMRT	Adjuvant post-RT PCV x 6
Astrocytoma	**3**	No 1p19q co-deletion	59.4 (54-55/30 if concern re very large volume e.g 2/3 of brain volume or organ at risk tolerances)	33	VMAT/IMRT	Adjuvant Temozolomide x 12
Ependymoma	**2, 3**	Consider Methylation for prognostication	60 59.4 54-55 (close proximity to brain stem)	30 33 30	VMAT/IMRT	No
Oligodendroglioma / Astrocytoma	**2**		54	30	VMAT/IMRT	Adjuvant PCV x 6
Pilocytic astrocytoma	**1**	Consider testing for BRAF mutation	50.4 - 54	28-30	VMAT/IMRT	No

Pituitary			45-47 50 (if large macroadeno ma, or specific aggressive histology)	25 30	VMAT/IMRT (stereotactic immobilisation is preferred)	
Craniopharyngioma		BRAF mutation	50	30	VMAT/IMRT (stereotactic immobilisation is preferred)	
Meningioma - skull base **Solitary fibrous tumour**	**1** **1**		50 (orbital or involving optic structures) 54 (e.g., non- skull base locations or if concerns re fast growth any location)	30 30	VMAT/IMAT (stereotactic immobilisation is preferred)	
Meningioma **Solitary fibrous tumour**	**2**	Consider Methylation for G2	55 59.4 60	30 33 30	VMAT/IMRT (stereotactic immobilisation is preferred)	
Meningioma **Solitary fibrous tumour**	**3**		60	30	VMAT/IMRT (stereotactic immobilisation is preferred)	
Chondrosarcoma/ chordoma			60 (66)	30 (33)	**Consider Proton therapy.** If photons use VMAT/IMRT with stereotactic immobilisation	

Clinical Indication (including treatment criteria)	**Grade / stage**	**Genetics**	**Dose (Gy)**	**Fractionation**	**Radiotherapy technique**	**Chemotherapy**
Pineal Germinoma (M0 & uni or bifocal) Whole ventricular RT +/-Boost to residual Follow SIOP protocol			24 16	15 10		Neoadjuvant CARBO/PEI x 4
Pineal NGGCT (post chemo CR, IF)			54	30	VMAT/IMRT	

Papillary Pineal body Tumour	**1**		54	30	VMAT/IMRT	
Haemangioblastoma			50-55	28 -30	VMAT /IMRT	
Vestibular schwannoma (>3cm diameter OR clinical signs of brainstem compression OR residual large volume disease post-surgery)			50-54	30	VMAT /IMRT (stereotactic immobilisation is required)	
High dose palliative any intracranial primary (if not suitable for above doses)			25	5	Conformal or VMAT/IMRT	
Retreatment Caution in using this following detailed evaluation of previous treatment dose, MDT discussion and MPE physics discussion			34-35 36-54 40	10 1.5-1.8Gy fraction sizes 15	VMAT/IMRT (stereotactic immobilisation is preferred)	minimum 1 year since previous treatment- see 'Retreatment of Central Nervous System Tumours', Jones, B. and Grant, W., Clinical Oncology, August 2014

3. Contouring Guidelines for Primary CNS Tumours

- Note that OAR PRV margin = 0.1-0.5 cm depending on local immobilisation audit data; PTV margin also determined by local immobilisation /imaging audit data and may vary from below.
- Consider pre op imaging, but take account of all anatomical changes following surgery
- For all stereotactic treatment the planning CT should be acquired with <=0.125cm slices.

Clinical Indication	GTV	CTV	PTV
Grade 1 Pilocytic Astrocytoma	GTV = POST-OP tumour volume on T1 +c	CTV = GTV	PTV = CTV + 0.5cm
Grade 2 Astrocytoma Oligodendroglioma Ependymoma	GTV = resection cavity and POST-OP tumour volume on T2 + FLAIR	CTV = GTV + 1.0cm-1.5cm or to anatomical boundary	PTV = CTV + 0.5cm
Grade 3 Astrocytoma Oligodendroglioma Ependymoma	GTV = post op residual T1+ gad enhancing tumour and resection cavity, include all abnormal tissue on T2 and FLAIR NB. For large volume tumours, T2 abnormality can be incorporated in GTV rather than CTV.	CTV = GTV + 1.0cm-1.5cm or to anatomical boundary	PTV = CTV + 0.5 cm
Grade 4 Astrocytoma Glioblastoma	GTV = T1 +gad post op residual tumour and resection cavity.	CTV = GTV + 1.5cm-2.0cm or to anatomical boundary (extend across midline if corpus callosum are involved) Extended to include T2/FLAIR for non-enhancing tumour element	PTV = CTV + 0.5 cm
Meningioma Grade 1 (use stereotactic treatment delivery in preference, particularly for all skull base meningiomas)	GTV = enhancing tumour (Consider local infiltration into bone and dural extension.) Contouring to be reviewed with/carried out in conjunction with neuroradiologist.	CTV = GTV + 0 - 0.2cm (up to 0.5cm depending on uncertainty especially if histologically unverified)	**PTV = CTV+0.5 cm** if standard immobilisation . **PTV= CTV + 0.3cm** if stereotactic system + standard mask **PTV = CTV + 0.1cm** if full stereotactic system + mask

Clinical Indication	GTV	CTV	PTV
Meningioma Grade 2 or 3 **Solitary fibrous tumour** (Use stereotactic treatment delivery in preference)	GTV = post op residual enhancing tumour and resection cavity. If bone is involved, a CT bone window setting is strongly advised. Clearly thickened dural tails and hyperostotic bones should be included whereas non-enhancing but thickened dura does not need to be included Contouring to be reviewed with/carried out in conjunction with neuroradiologist.	CTV = GTV + sub-clinical microscopic tumour which may include the pre-operative tumour bed, peritumoural oedema, hyperostotic bone changes, and dural enhancement or thickening as seen in the CT/MRI at diagnosis. An additional 3-dimensional margin of **1.0 cm along the meninges** should be added limited by the patient skin surface. The margin should be reduced to **0.5 cm elsewhere,** including where this would extend into brain tissue unless there is evidence of invasion when the **1.0 cm margin should be maintained.**	**PTV = CTV+0.5 cm** if standard immobilisation . **PTV= CTV + 0.3cm** if stereotactic delivery system + standard mask **PTV = CTV + 0.1cm** if full stereotactic delivery system + mask
Vestibular schwannoma (Use stereotactic treatment delivery in preference)	Enhancing and cystic tumour Contouring to be reviewed with/carried out in conjunction with neuroradiologist.	CTV=GTV	**PTV = CTV+0.5 cm** if standard immobilisation . **PTV= CTV + 0.3cm** if stereotactic delivery system + standard mask **PTV = CTV + 0.1cm** if full stereotactic delivery system + mask
Pituitary (Use stereotactic treatment delivery in preference)	GTV = POST-OP tumour volume Contouring to be carried out in conjunction with neuroradiologist.	CTV = GTV + 0 - 0.5cm depending on contouring uncertainty	**PTV = CTV+0.5 cm** if standard immobilisation . **PTV= CTV + 0.3cm** if stereotactic delivery system + standard mask **PTV = CTV + 0.1cm** if full stereotactic delivery system + mask

Craniopharyngioma (Use stereotactic treatment delivery in preference)	GTV = POST-OP tumour volume, consider post and pre op tumour volume imaging and cystic portion, ensure entire tumour bed is contoured Contouring to be carried out in conjunctions with neuroradiologist.	CTV = GTV + 0-0.5cm depending on cystic expansion potential	**PTV = CTV+0.5 cm** if standard immobilisation . **PTV= CTV + 0.3cm** if stereotactic delivery system + standard mask **PTV = CTV + 0.1cm** if full stereotactic delivery system + mask

Clinical Indication	GTV	CTV	PTV
Pineocytoma	GTV = visible residual tumour and /or tumour bed	CTV = GTV + 0.5-1cm	PTV = CTV + 0.5cm
Pineal Germinoma (uni or bi focal, M0) **For metastatic disease use craniospinal irradiation (see whole CNS RT protocol).**	Phase 1: Craniospinal axis/Whole ventricular system Phase 2: Visible tumour/tumour bed	Phase 1: CTV = GTV + 0.5cm Phase 2: CTV = GTV + 1cm	PTV = CTV + 0.5cm
Reirradiation of primary brain tumours (Use stereotactic treatment delivery in preference)	All visible disease. Contouring to be carried out in conjunctions with neuroradiologist.	CTV= GTV+ 0-1cm	**PTV = CTV+0.5 cm** if standard immobilisation . **PTV= CTV + 0.3cm** if stereotactic delivery system + standard mask **PTV = CTV + 0.1cm** if full stereotactic delivery system + mask

4. Normal Tissue Dose Constraints (non- SRS)

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 < 0.1cm^3		Mean dose
	Optimal	Mandatory	
Cord PRV	48 Gy	50 Gy	
Brainstem PRV†	54 Gy	V>54Gy < 10cc D0.1cm^3 < 59Gy, (absolute volume receiving 59Gy <= 10 cm^3) risk <5%	
Optic nerves/ chiasm PRV	54 Gy	54Gy	
Orbit PRV (Retina)	45 Gy	50Gy	
PTV coverage should NOT be compromised to meet the constraints shown below:			
Lacrimal gland	≤30Gy	*	
Brain-CTV	60Gy (D1cc)		
Lenses	6 Gy	10Gy	
Cochlea (ipsilateral)	-	-	45Gy Spare contralateral cochlea – keep mean dose below 10-25 Gy
Whole Parotid	-	-	Below24Gy
Bilateral Hippocampi (where tumour not involving either side) = hippocampal avoidance zone	-	-	Aim for EQD2 to 40% of bilateral hippocampi (hippocampal avoidance zone <7.3Gy) – Failure to achieve this ideal constraint should not compromise PTV coverage. To optimise.
Unilateral non affected hippocampus (where tumour directly involving one hippocampus)	-	-	Aim for avoidance of contralateral hippocampal avoidance zone – again as low as achievable. To optimise.

Appendix 1: Specific Guidelines for Vestibular Schwannoma Delineation (from the Christie Protocol)

The GTV is the gross (visible) tumour. Usually this will be clearer on MRI than on CT, although the CT is the primary dataset for patient positioning. However, the T1+gadolinium MRI sequence may suffer from geometric distortion and overestimation of the target volume. The GTV outline should therefore also be evaluated with respect to the thin slice FIESTA sequence, which is less prone to these effects. The GTV will usually be drawn to cover the T1+gad extent, but where the tumour is close to or abutting brainstem, covering only the FIESTA extent may be preferable in order to limit brainstem dose. The GTV should also be reviewed on the CT with bone windows, as the intracanalicular part should fit the bony anatomy of the IAC. This is especially critical when it is desired to preserve useful hearing, because the IAC is very close to the cochlea. Overestimation of the intracanalicular part will increase the cochlear dose. In addition, the facial and cochlear nerve usually run along the anterior border of the tumour in the IAC, so that making the volume too large anteriorly may move the nerves into the higher dose region, making them more susceptible to damage.
However, this is likely to be much less critical than with Gamma Knife, which has much steeper dose gradients within the PTV.

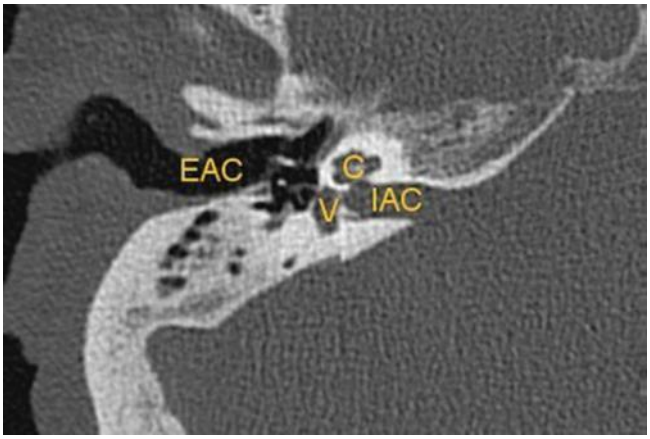

Figure 1. Axial CT through skull base. IAC, internal auditory canal, EAC, external auditory canal, C, cochlea, V, vestibule (Bhandare et al., 2010)

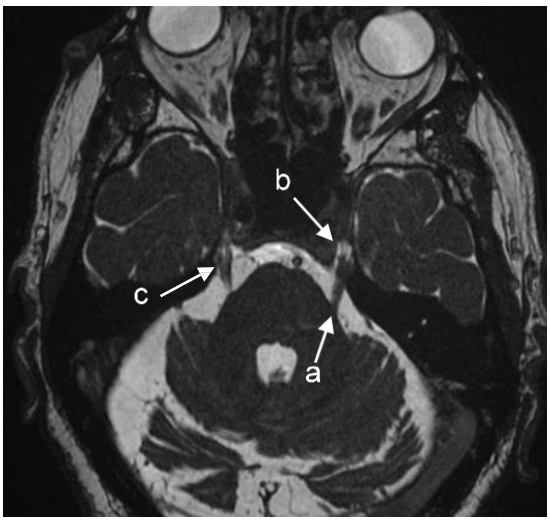

Figure 2. FIESTA sequence, 0.4 mm slices. The left trigeminal nerve is seen exiting the brainstem (a) and entering Meckel's cave (b). The right trigeminal nerve is also seen (c). (SRFT imaging).

Appendix 2: Diagnostic imaging requirements for pre-treatment imaging

REQUEST STANDARD MRI HEAD FOR ALL CASES FOR FUSION WITH PLANNING CT SCAN.

Site	MRI sequences to be requested	CT (if MRI contraindicated) sequences to be requested
Skull base or orbital Meningioma	High res skull base protocol including high res axial 3 mm T1 fat sat post gad. (If done on 3T magnet, volume T1 post gad sequence should also be included.) Standard MRI head for fusion with planning CT.	Helical acquisition post contrast with bone algorithm reconstructions in 3 planes at 1 mm slice thickness and soft tissue algorithm reconstructions in 3 planes at 3 mm slice thickness
Pituitary Adenoma	Pituitary protocol + including high res. axial 3 mm T1 fat sat post gad. (If done on 3T magnet, volume T1 post gad sequence should also be included.) Standard MRI head for fusion with planning CT.	Helical acquisition post contrast with bone algorithm reconstructions in 3 planes at 1 mm slice thickness and soft tissue algorithm reconstructions in 3 planes at 3 mm slice thickness
Craniopharyngioma	Pituitary protocol + including high res axial 3 mm T1 fat sat post gad. (If done on 3T magnet, volume T1 post gad sequence should also be included.) Standard MRI head for fusion with planning CT.	Helical acquisition post contrast with bone algorithm reconstructions in 3 planes at 1 mm slice thickness and soft tissue algorithm reconstructions in 3 planes at 3 mm slice thickness
Vestibular Schwannoma	Post Gad axial FIESTA (GE scanners) or balanced FFE (Philips scanner) (If done on 3T magnet, volume T1 post gad sequence could also be included.) Standard MRI head for fusion with planning CT.	Helical acquisition post contrast with bone algorithm reconstructions in 3 planes at 1 mm slice thickness and soft tissue algorithm reconstructions in 3 planes at 3 mm slice thickness
Skull Base Glomus/paragangliomata	High res skull base protocol including high res axial 3 mm T1 fat sat post gad. (If done on 3T magnet, volume T1 post gad sequence should also be included.) Standard MRI head for fusion with planning CT.	Helical acquisition post contrast with bone algorithm reconstructions in 3 planes at 1 mm slice thickness and soft tissue algorithm reconstructions in 3 planes at 3 mm slice thickness
CNS Metastases	Volume T1 brain post gad in axial plane (e.g. FMSPGR on 3T GE scanners or STEALTH T1 on 1.5T Philips scanner.)	Helical acquisition post contrast with soft tissue algorithm reconstructions in 3 planes at 3 mm slice thickness