East of England Radiotherapy Network:

Central Nervous System Protocol V3.0

Contents

1. Primary Brain Tumours

1.1. Indications and patient population

This protocol covers treatment in the following situations, with reference to NICE guideline NG99 where appropriate[1]:

A. Radical radiotherapy for high grade glioma (CNS WHO grade 3 and 4)

Following maximal safe resection or biopsy of grade 4 glioma:

- Offer radiotherapy 60 Gy in 30 fractions with concomitant temozolomide and up to 6 cycles of adjuvant temozolomide to people aged around 70 or under who are KPS ≥ 70
- Offer radiotherapy 40 Gy in 15 fractions with concomitant temozolomide and up to 12 cycles of adjuvant temozolomide to people aged around 70 or over who are KPS ≥ 70 and have MGMT promoter methylation
- Offer radiotherapy 40 Gy in 15 fractions alone or primary temozolomide chemotherapy to people aged around 70 or over who are KPS ≥ 70 and do not have MGMT promoter methylation. Consider concomitant and up to 12 cycles of adjuvant temozolomide in select cases with borderline MGMT promoter methylation

Following surgery for grade 3 glioma:

- Offer sequential radiotherapy and 4 to 6 cycles of PCV chemotherapy to people with grade 3 glioma with 1p/19q codeletion (oligodendroglioma), after discussing the order of PCV and radiotherapy
- Offer radiotherapy followed by 12 cycles of adjuvant temozolomide to people with grade 3 astrocytoma

B. Radical radiotherapy for low grade glioma (CNS WHO grade 2)

Following surgery for grade 2 glioma:

- Offer radiotherapy followed by up to 6 cycles of PCV for people who have a grade 2 glioma with 1p/19q codeletion (oligodendroglioma) and are aged around 40 or over or have residual tumour on postoperative MRI
- Consider radiotherapy followed by up to 6 cycles of PCV for people who have a grade 2 astrocytoma and are aged around 40 or over or have residual tumour on postoperative MRI. These patients may alternatively be offered adjuvant temozolomide chemotherapy (outside of NICE guidelines)
- Consider radiotherapy followed by up to 6 cycles of PCV for people who are radiotherapy-naïve if they have progressive disease on radiological follow-up or intractable seizures
- Consider active monitoring for people who are aged around 40 or under and no residual tumour on postoperative MRI

C. Palliative radiotherapy for high grade glioma

Consider radiotherapy alone (60 Gy in 30 fractions), hypofractionated radiotherapy or best supportive care for patients not covered by (A) and (B).

D. Re-irradiation for glioma with localised disease recurrence

For focally recurrent high-grade glioma, the treatment options of further surgery, chemotherapy, radiotherapy and best supportive care should be considered. For re-irradiation, the modified Combs criteria can be a useful prognostic score to guide decision-making[2,3]. This takes into account:

- Primary histology (G1/2 vs G3 vs G4)
- Age (<50 vs ≥50 years)
- Time from primary radiotherapy (>12 vs ≤12 months)
- Re-resection performed (yes vs no)
- KPS (≥80 vs <80)
- PTV volume (≤47 vs >47 ml)

E. Radical radiotherapy for meningioma

For asymptomatic incidental meningioma, scan at 12 months and if stable appearances consider discharge or scan at 5 years as per NICE guidelines[1]. For patients undergoing surgical resection, the extent of resection (Simpson grade) should be documented.

- G1 meningioma: consider radiotherapy or surveillance for incomplete resection, taking into account the consequences of recurrence, ease of re-operation and patient factors/preferences
- G2 meningioma: radiotherapy is indicated after incomplete resection. For complete resection, surveillance can be offered as per G1 meningioma (the ROAM/EORTC-1308 trial[4] is currently in follow-up)
- G3 meningioma: adjuvant radiotherapy is indicated

F. Radical radiotherapy for ependymoma

Whenever feasible, gross total resection is recommended. Staging should include craniospinal MRI and CSF cytology. Postoperative radiotherapy is recommended for patients with incompletely-resected grade 2 ependymoma and all patients with grade 3 ependymoma[5]. For patients with CSF or spinal dissemination, CSA RT is recommended.

G. Radical/adjuvant radiotherapy for pituitary tumours including craniopharyngioma

All patients should be discussed in a pituitary MDT. The need for radiotherapy is judged on an individual basis, taking into account surgical findings, imaging, pathology, tumour hormone production, age, performance status and current HPA axis function.

For pituitary adenoma, consider radiotherapy for:

- Extensive postoperative residuum
- Invasion of the cavernous sinus(es)
- Uncontrolled elevated hormone levels
- Progressive disease following surgery

For craniopharyngioma, radical surgery can be associated with significant morbidity. Therefore, often a subtotal resection followed by postoperative radiotherapy is planned which results in good local control with less toxicity.

H. Radiotherapy for medulloblastoma, supratentorial PNET, pineoblastoma and intracranial germinoma

Staging should include craniospinal MRI and CSF cytology along with serum HCG and AFP. Treatment involves whole CSA RT with a boost to the primary region; patients should be considered for referral for PBT.

I. Radical radiotherapy for vestibular schwannoma

All patients should be discussed in the skull base MDT. Management options include:

- Surveillance for small tumours without evidence of radiological progression or brainstem compression
- Surgery
- Stereotactic radiosurgery for smaller tumours without indentation of the brainstem
- Fractionated radiotherapy

J. Radical radiotherapy for paraganglioma (glomus tumours)

The decision between surgery and radiotherapy is judged on an individual patient basis. Surgery results in removal of the tumour (aiming for complete resection) at the risk of neurological deficits. Radiotherapy is well-tolerated, but the tumour remains, and there is the potential for late radiotherapy side-effects including the very low risk of second malignancy.

K. Radical and palliative radiotherapy for chordoma and chondrosarcoma

These tumours are relatively radio-resistant requiring high doses of radiotherapy balanced with normal tissue dose. Following debulking surgery patients should be considered for Proton Beam Therapy. For patients unsuitable for PBT (including due to the presence of metal implants required for spinal reconstruction), fractionated photon therapy can be considered. Palliative treatment may still require high doses.

L. Radical/adjuvant radiotherapy for spinal cord tumours

Primary malignant spinal cord tumours are usually intrinsic. Gliomas (astrocytoma or glioblastoma) will usually lend themselves to biopsy or debulking with postoperative radiotherapy therefore indicated. Surveillance can be considered for patients with grade 1 subependymoma or myxopapillary ependymoma following complete resection.

1.2. Treatment eligibility

1.2.1. Inclusion criteria

- Adequate performance status and physiological reserve
- Adequate cognitive function
- Able to provide informed consent for treatment

1.2.2. Exclusion criteria

- Inadequate cognitive function/mental capacity issues for safe delivery of radiotherapy
- Unable to tolerate immobilisation required to deliver radiotherapy

1.2.3. Essential pre-radiotherapy investigations for curative patients

- Bloods: FBC, U&E, LFTs for patients that require IV contrast imaging studies (planning CT / MRI) or are planned for chemotherapy
- Fertility should be discussed (egg preservation and sperm banking) and referrals should be sent to appropriate centres
- Patient receiving chemo-radiation treatment should have a chemotherapy plan prescribed in advance

1.3. Localisation

Localisation	Options	Notes
Position	Cranial (including skull base)	Supine with head straight in a neutral position
	Spinal: cervical lesions	Supine with head straight in a neutral position
	Spinal: thoracic lesions	Supine, consider chest pole with arms raised
	Spinal: lumbar/sacral lesions	Supine; patients in pain may need to be treated in a prone position for comfort
Immobilisation and supports	Cranial (including skull base)	Thermoplastic beam direction shell with either 5- or 9-point fixation
	Spinal: cervical lesions	Thermoplastic shell
	Spinal: thoracic lesions	Consider chest pole with arms raised
	Spinal: lumbar/sacral lesions	Knee rest and ankle stocks
Contrast	Cranial	Unenhanced scan, IV contrast can be considered if no planning MR
CT acquisition	Slice thickness	1-3mm (1-2 mm for skull base lesions)
	Scanning limits	Vertex to the bottom of C3
MRI brain protocol	High grade planning	Axial T2, 3 mm, whole brain Axial T1+Gad, 3 mm, whole brain Sagittal T1, 3 mm, whole brain Axial FLAIR, 3mm, whole brain
	Low grade planning	Axial T2, 3 mm, whole brain Axial T1+Gad, 3 mm, whole brain (not required but part of standard glioma protocol) Sagittal T1, 3 mm, whole brain Axial FLAIR, 3mm, whole brain
	Tumours within or close to optic pathways	Axial T2, 3 mm, whole brain Axial T1+Gad, 1 mm, whole brain Axial LAVA Flex, 1 mm
	Skull base for stereotactic radiosurgery/SRS meningioma	Axial T1+Gad, 1 mm, whole brain (3D geometry correction enabled) (3DT1w BRAVO+C) Axial 3D FIESTA+Gad, 1 mm, whole brain (3D geometry correction enabled) Volumetric FLAIR reconstructed in Axial, 1mm (3D geometry correction enabled) Axial reformat of 3D FLAIR

1.4. Dose prescription & chemotherapy

Intent	Dose (Gy)/#	#/ week	Comments
Radical radiotherapy for grade 4 glioma	60 Gy / 30#	5/week	Concomitant temozolomide 75 mg/m^2 (7 days per week) 6 cycles of adjuvant temozolomide 150-200 mg/m^2 (D1-5 q28d)
	40 Gy / 15#		Concomitant temozolomide 75 mg/m^2 (7 days per week) 6-12 cycles of adjuvant temozolomide 150-200 mg/m^2 (D1-5 q28d) If MGMT unmethylated and age >70 years then no temozolomide
Radical radiotherapy for grade 3 glioma	59.4 Gy / 33#	5/week	Astrocytoma: 12 cycles of adjuvant temozolomide 150-200 mg/m^2 (D1-5 q28d)
			Oligodendroglioma, 1p/19q codeleted: 4-6 cycles of adjuvant PCV
Palliative radiotherapy for high grade glioma	30 Gy / 6#	3/week	
	34 Gy / 10#	5/week	
Radical radiotherapy for grade 2 oligodendroglioma, 1p/19q codeleted	54 Gy / 30#	5/week	4-6 cycles of adjuvant PCV
	50.4 Gy / 28#		
Radical radiotherapy for grade 2 astrocytoma	54 Gy / 30#	5/week	4-6 cycles of adjuvant PCV Patients may be offered temozolomide instead of PCV (outside of NICE guidelines)
	50.4 Gy / 28#		
	59.4 Gy / 33#		
Re-irradiation for glioma with localised disease recurrence	36 Gy / 12#	5/week	Consider 35 Gy / 10# for GTV greater than 47cc
	35 Gy / 10#		
Radical radiotherapy for grade 1 meningioma	50 Gy / 30#	5/week	Adjuvant radiotherapy when indicated
	50.4 Gy / 28#		
	54 Gy / 30#		
	55 Gy / 33#		
Radical radiotherapy for grade 2 meningioma	54 Gy / 30#	5/week	Adjuvant radiotherapy when indicated
	55 Gy / 33#		
	60 Gy / 30#		
Radical radiotherapy for grade 3 meningioma	60 Gy / 30#	5/week	Adjuvant radiotherapy is indicated

Intent	Dose (Gy)/#	#/ week	Comments
Radical radiotherapy for ependymoma	54 Gy / 30#	5/week	CNS WHO grade 2 (can be observed if complete resection)
	59.4 Gy / 33#		CNS WHO grade 3
Radical/adjuvant radiotherapy for pituitary tumours	45 Gy / 25#	5/week	Standard dose
	50 Gy / 30#		Very large or invasive tumours
	55 Gy / 33#		Pituitary carcinoma
	54 Gy / 27-30#		Standard dose
Radical/adjuvant radiotherapy for craniopharyngioma	50 Gy / 30#	5/week	Standard dose
	55 Gy / 33#		Aggressive tumours (residual tumour or tumour progression post-surgery, invasion of cavernous sinuses, uncontrolled hormones levels) Historical studies show 55Gy for local control, though concern over the risk of radiation induced optic neuropathy has resulted in median doses of 50-52.2 Gy
	50.4 Gy / 28#		Standard dose
	52.2 Gy / 27#		Standard dose
Medulloblastoma	36 Gy / 20#	5/week	Followed by boost to primary site and any focal spinal metastases:
Cranial boost	19.8 Gy / 11#	5/week	Whole posterior cranial fossa for metastatic medulloblastoma
Spinal boost (diffuse spinal cord metastases)	3.6 Gy / 2#	2/week	
Focal spinal cord boost	9 Gy / 5#	5/week	Above the termination of the spinal cord
	14.4 Gy / 8#		Below the termination of the spinal cord
Diffuse leptomeningeal disease	54 Gy /30#	5/week	Phase 1 whole CSA: 39.6 Gy / 22# Phase 2 boost: 14.4 Gy / 8#
Germinoma	40 Gy / 24#	5/week	Phase 1 whole CSA: 25Gy / 15# Phase 2 boost: 15 Gy / 9#
Pineoblastoma	55 Gy / 33#	5/week	Phase 1 whole CSA: 35 Gy / 21# Phase 2 boost: 20 Gy / 12#
Vestibular schwannoma	12 Gy / 1#	5/week	SRS where indicated
	50 Gy / 30#		Fractionated radiotherapy
Paraganglioma (glomus tumours)	50 Gy / 30#	5/week	

Intent	Dose (Gy)/#	#/ week	Comments
Chordoma and chondrosarcoma unsuitable for PBT	65-70 Gy / 39#	5/week	
Spinal cord tumours	50 Gy / 30#	5/week	Ependymoma and astrocytoma histology
	55 Gy / 33#		
	50.4-54 Gy /30#		Glioblastoma
	54-60 Gy / 30#		Cauda equina glioblastoma
	50 Gy / 30#		Meningioma, schwannoma

1.5. Target volumes

Use standard nomenclature as per AAPM 263[6]. Refer to local policy for PTV margins. Useful related guidelines include:

- ESTRO-EANO guideline on target delineation and radiotherapy details for glioblastoma[7]
- ESTRO-EANO guideline on target delineation and radiotherapy for IDH-mutant WHO CNS grade 2 and 3 diffuse glioma[8]
- ESTRO ACROP guideline for target volume delineation of skull base tumors[9]

1.5.1. Radical radiotherapy for high grade glioma

MRI produces superior definition of tumour, and the planning MRI should be co-registered to the planning CT.

GTV: This is defined as the resection cavity plus any residual contrast-enhancing tumour on T1W+Gad. Some regions of contrast enhancement may represent post-surgical infarction or gliosis; these areas may be excluded from the GTV after careful review of pre- and immediate post-resection MRI scans including diffusion-weighted imaging (DWI).

Where T2/FLAIR hyperintensity is felt to represent oedema, it should not be included in the GTV. However, where these signal changes are felt to represent non-enhancing tumour, they should be encompassed in the GTV.

CTV: GTV + 15 mm. Margins should be reduced at anatomical barriers such as the skull (0 mm, using bone windows), ventricles (5 mm), falx (0 mm), tentorium cerebelli (0 mm), visual pathways/optic chiasm (0 mm) and brainstem (0 mm) provided the tumour is distant from white matter tracts extending to these regions. No margin reduction should be applied at the corpus callosum, cerebral and cerebellar peduncles; if tumour extends to the contralateral hemisphere or infiltrates the corpus callosum the CTV should cross the midline.

1.5.2. Radical radiotherapy for low grade glioma

GTV: This should encompass the full extent of visible abnormality demonstrated on T2W and T2/FLAIR sequences. For patients who have undergone surgery, the resection cavity should also be included in the GTV.

CTV: GTV + 10 mm. This should be edited as per high grade glioma.

1.5.3. Re-irradiation of glioma

GTV: This should be delineated as the extent of visible abnormality as demonstrated on the T1W+Gad sequence. For patients who have undergone debulking surgery the GTV should represent the post operative residual disease.

CTV: Allow a small margin in the region of 5-10 mm.

1.5.4. Meningioma

MRI using a T1W sequence with gadolinium contrast produces optimal localization of the tumour. CT shows the limits of meningioma extension up to bone or, in uncommon cases where the tumour involves the bone, the extent of the invasion. CT also shows the foramina and fissures of the skull,

through which meningiomas can spread. When resection has been carried out, co-registration of the preoperative MRI is required.

GTV: This is defined as the area of abnormality or any residual tumour and the resection cavity (if available) as demonstrated on the T1W+Gad post op MRI sequence, without inclusion of the perilesional oedema. T2-weighted sequences can also be useful to assess the extent of peritumoral oedema and dural tail abnormalities. Care must be taken to include tumour infiltration of the meninges; thickened dural tail should be included in the GTV. Only directly invaded bone and clearly hyperostotic bone should be included in the GTV using a CT bone window to improve target delineation.

CTV: There is little hard evidence for the size of CTV margin that should be used. For an individual tumour, its growth pattern suggests whether a small or large margin is needed, including whether there is brain or bony invasion. Contouring the preoperative GTV to show the location of the tumour will ensure that the base of the lesion (i.e. meningeal surfaces into which spread might occur) is included.

Grade 1:	CTV = GTV
Grade 2:	along the meninges: CTV = GTV + 5-10 mm at other surfaces: CTV = GTV
Grade 3:	along the meninges: CTV = GTV + 10-20 mm including the preoperative tumour bed, peritumoural oedema, hyperostotic bone changes and dural enhancement/thickening at other surfaces: CTV = GTV + 5-10 mm around natural barriers to tumour growth e.g. skull base unless there is evidence of invasion.

1.5.5. Ependymoma

Pre and postoperative MRI T1 weighted images should be co-registered with the planning CT.

Posterior fossa tumours

GTV: Any residual postoperative tumour as demonstrated on T1W+Gad

CTV: Post-operative cavity allowing 10-20 mm for all low- and high-grade. Consider the whole posterior fossa as CTV

Supratentorial tumours

GTV: Any residual postoperative tumour as demonstrated on T1W+Gad

CTV: GTV + 15-25 mm (dependent on grade)

1.5.6. Pituitary tumours

Pituitary adenoma

GTV: Residual tumour defined as the contrast-enhancing abnormality, best shown on MRI, using pre- and post-contrast enhanced T1-weighted sequences, with inferior limit determined by bony structures of the skull base on CT. It is not necessary to treat surgical packing in the sphenoid, but occasionally tumours do invade the sphenoid.

In addition, preoperative and contrast-enhanced T1-weighted images may be helpful to discern postoperative changes from the tumour, especially in patients who have undergone several surgeries.

CTV: Normally this includes the whole pituitary fossa where the original tumour was located. There is no need to include areas of superior extension which have been surgically removed (opposite to craniopharyngioma, see below). Adenomas do not infiltrate at a microscopic level.

Additional margin expansion from GTV to CTV is usually unnecessary. A margin of 2-3 mm may be added in case of invasive and aggressive pituitary tumours to encompass all potential areas of microscopic tumour infiltration, e.g. fast-growing tumours invading the cavernous sinus.

Craniopharyngioma

GTV: Craniopharyngiomas are difficult to contour. Post-contrast T1- weighted and T2-weighted MRI sequences are essential to demonstrate the extent of the GTV. Usually there are post-operative solid or cystic remnants. If so, these represent GTV. The solid portion of craniopharyngiomas is more precisely contoured using the contrast-enhanced T1-weighted images, whereas fast T2-weighted images allow for better visualization of cystic components of the tumour.

Note: occasionally the planning MR demonstrates cystic recurrence. This requires immediate neurosurgical discussion, for consideration of further surgery.

CTV: GTV + 3-5mm margin, to take into account potential microscopic areas of tumour infiltration and changes of cystic components of the tumour during the treatment that may occur in up to 40% of patients.

The tumour is very adherent at both a macroscopic and microscopic level. Contouring may be facilitated by co-registered pre-operative MRI imaging, remembering that resection decompresses the tumour, reduces the mass effect, and shifts the anatomy.

1.5.7. Vestibular Schwannoma

Fast imaging employing steady-state acquisition (FIESTA) sequences may be useful for improving the visualisation of the cisternal segments of cranial nerves.

GTV: The enhancing lesion as demonstrated on T1W+Gad MRI. In addition, bony CT windows are helpful since the enlargement of vestibular canal can be visible representing the tumour volume

CTV: CTV = GTV

1.5.8. Germinoma

Phase 1 should treat the craniospinal axis, and this is most effectively planned from CT.

Phase 2 GTV is the contrast-enhancing tumour in MRI T1W**.** CTV is 10-20 mm, grown isotropically.

1.5.9. Medulloblastoma in adults

Phase 1 should treat the craniospinal axis, and this is most effectively planned from CT.

CTV: for all the tumours requiring whole CSA Radiotherapy

- Cranial: needs to include all meningeal reflections, including all the skull foramina, the optic nerves and the cribriform plate

- Spinal: should include the nerve roots as they exit from the foramina and the full extent of the spinal cord, including the filum terminale, which is likely to require the inferior aspect of the field to extend to around S1/2.

Phase 2

GTV: is the contrast-enhancing tumour in MRI T1W

CTV: Encompasses the entire posterior fossa (multifocal or high-risk disease). In standard risk patients with complete disease resection in a central location the volume may be reduced to comprise the tumour bed with a margin of 15 mm.

1.5.10. Paragangliomas (Glomus Tumour)

GTV: the enhancing lesion as demonstrated on T1W+Gad MRI sequence

CTV: GTV (consider an additional margin of 1-2 mm if there are imaging uncertainties)

1.5.11. Chordomas and Chordosarcomas

GTV: the enhancing lesion as demonstrated on T1W+Gad and/or T2W MRI sequence(s).

CTV: GTV + few mm. Should encompass all potential areas at risk of microscopic spread of disease (There is no published evidence base for the size of this margin, but the experience here is that these margins can reflect the invasiveness of the tumour seen on pre-operative imaging). CTV can be restricted to the intact cortex**.**

1.5.12. Spinal Cord Tumours

GTV: includes the residual tumour visible on the T1 enhancing abnormality on MRI or the tumour on T2/FLAIR images if they are low grade gliomas. The post-operative cavity should be included in the GTV. Whole width of the cord over a length equal to the extent of the preoperative GTV (best demonstrated on pre-op MRI).

CTV: Oedema on a T2 weighted MRI with a margin of 15 mm for low grade tumours, and 20-30 mm for high grade tumours around the GTV to include any subclinical spread, depending on the histology and the location of the tumour. When the vertebrae body is involved, this should be included in the CTV.

Ependymoma: wider than the cord, to ensure coverage of the whole spinal canal, including nerve root extensions of dura.

Longitudinally GTV + 20 mm proximally and distally

PTV: For radical treatments PTV = CTV + 3-5 mm. For palliative treatments CTV + 3-5 mm or GTV + 10 mm

1.6. Organs at risk

Use standard nomenclature as per the Global Harmonization Group consensus guidelines[10]. There are several consensus-based atlases for OAR delineation in neuro-oncology[11–13].

Structure name	Description
Eye_L or _R **Eye_A_L or _A_R** **Eye_P_L or P_R**	Anterior segment of the eyeball: The anterior segment of the eyeball consists of the structures ventral from the vitreous humour, including the cornea, iris, ciliary body, and lens. Posterior segment of the eyeball: The posterior segment of the eyeball is located posteriorly to the lens and consists of the anterior hyaloid membrane and all of the posterior optical structures including the vitreous humour, retina, and choroid. The optic nerve is excluded from this contour. The entire retina is included in the posterior segment of the eyeball.
Glnd_Lacrimal_L or _R	The lacrimal gland is an almond-shaped gland located in the orbit supero-lateral to the eye, superior to the lateral rectus muscle and lateral to the superior rectus muscle. It can be delineated on CT using soft brain 120/40 or soft tissue 350/50 WW/WL settings
Lens_L or _R	A biconvex avascular structure in the T1-precontrast MRI. Located between the vitreous and the iris.
OpticNrv_L or _R	Left optic nerve and right optic nerve. 2-5 mm thick. The optic nerve is delineated from the posterior edge of eyeball to the optic chiasm. Visible on both MRI and CT, the latter useful for the relationship with bony optic canal.
OpticNrv_L_PRV or _R_PRV	A Planning Risk Volume (PRV) is created to account for positioning error using an appropriate margin, usually 2-3 mm isotropic.
OpticChiasm	Use CT in the cerebral window/level: even without contrast, it is hyperdense and on MRI T1 and T2-weighted images, it is hyperintense. The position of the optic chiasm is related to the position of the brain. In 80% of the cases is found superior to the 2/3 posterior of the sella. Delineation: Start just medial to the anterior clinoid process. Optic chiasm lies just anterior to the pituitary stalk and superior to the sella turcica, crossing just anterior to the pituitary stalk and the mammillary bodies. In the sagittal views is located in the end of laminal terminalis. In the coronal views the optic chiasm is located above the pituitary stalk. The last slice is in the level of the pons and it lies between the third ventricle.
OpticChiasm_PRV	A Planning Risk Volume (PRV) is created to account for positioning error using an appropriate margin, usually 2-3 mm.
Cochlea_L or _R	Delineation in the T1 pre-contrast MRI scan follow the VIII cranial nerve which separates the cochlea from the labyrinth, above is the cochlea and below is the labyrinth. It is located in the end of the nerve.
Hippocampus_L or _R	T1-weighted MRI or use the PD T2-weighted MRI. MRI slices along the axis of the hippocampus allows better visualisation. Sagittal imaging demonstrated as a banana shape, located in the plane of the lateral ventricle
Brainstem	Delineate in CT scan: cerebral window/level or in the MRI:T1-weighted images. Sagittal plane can be useful. The brainstem comprises the midbrain, pons and medulla Upper border: posterior clinoid and the inferior border: foramen magnum.

	The volume of the brainstem can be affected by surgery and neurodegenerative conditions. Number of surgeries, hydrocephalus, diabetes, and hypertension.
Brainstem_PRV	A Planning Risk Volume (PRV) is created to account for positioning error using an appropriate margin, usually 2-4 mm isotropically.
Pituitary	The pituitary gland appears as an oval-shaped structure within the sella turcica of the sphenoid bone. Laterally, it is bordered by the cavernous sinuses. It is just inferior to the brain, and is connected to the hypothalamus by its pituitary stalk.

1.7. Dose constraints

We are aiming to achieve dose constraints to the PRV for the brainstem, optic chiasm and optic nerve. If required we can report to the structure i.e. overlap of PRV OAR with tumour.

1.7.1. 60 Gy in 30#

Structure name	Constraint	Optimal	Mandatory
Brainstem_PRV	D0.1cc	< 54 Gy	59 Gy
	V54Gy		< 10cc
Lens_L or _R	D0.1cc	< 6 Gy	< 10 Gy
Eye_L or _R	D0.1cc	< 40 Gy	
Cornea_L or _R	D0.1cc	30 Gy	
Cochlea_L or _R	Dmean	< 40 Gy to ipsilateral cochlea & < 10 Gy to contralateral cochlea (COSTAR)	
Glnd_Lacrimal_L or _R	D0.1cc	< 26Gy	
OpticNrv_L_PRV or _R_PRV	D0.1cc	< 50 Gy	< 54-55 Gy to whole structure
OpticChiasm_PRV	D0.1cc	< 50Gy	< 54-55 Gy to whole structure
Pituitary	D0.1cc	< 45 Gy to whole gland	
SpinalCord_PRV	D0.1cc	< 48 Gy	< 50 Gy
Parotid_L or _R	Dmean	< 20 Gy	
Lobe_Temporal_L or _R	V60Gy	< 5.5 cc	
Bone_Mandible	D0.1cc	< 50 Gy	< 60 Gy
Hippocampus_L or _R	D40% Dmean	< 7.3 Gy < 30 Gy	

1.7.2. 50 Gy in 30#

Structure name	Constraint	Optimal	Mandatory
Brainstem_PRV	D0.1cc	< 48 Gy	< 51.5 Gy
Lens_L or _R	D0.1cc	< 6 Gy	< 10 Gy
Eye_L or _R	D0.1cc	< 40 Gy	

Cornea_L or _R	D0.1cc	< 30 Gy	
Cochlea _L or _R	Dmean	Mean dose < 40 Gy to ipsilateral cochlea and < 10 Gy to contralateral cochlea (COSTAR)	
Glnd_Lacrimal_L or _R	D0.1cc V30Gy	< 26Gy < 50%	
OpticNrv_L_PRV or _R_PRV	D0.1cc	< 48 Gy	< 51.5 Gy
OpticChiasm_PRV	D0.1cc	< 48Gy	< 51.5 Gy
Pituitary	D0.1cc	< 45 Gy	
SpinalCord_PRV	D0.1cc	< 48 Gy	< 51.5 Gy
Parotid_L or _R	Dmean	< 20 Gy	
Bone_Mandible	D0.1cc	< 50 Gy	
Hippocampus_L or _R	D40% Dmean	< 7.3 Gy < 30 Gy	

1.7.3. 40 Gy in 15#

Structure name	Constraint	Optimal	Mandatory
Brainstem_PRV	D0.1cc		< 40 Gy
Lens_L or _R	D0.1cc		< 4 Gy
Eye_L or _R	D0.1cc	< 40 Gy	
Cornea_L or _R	D0.1cc	< 30 Gy	
Cochlea_L or _R	Dmean	< 39 Gy	
Glnd_Lacrimal_L or _R	D0.1cc	< 22Gy	
OpticNrv_L_PRV or _R_PRV	D0.1cc		< 40 Gy
OpticChiasm_PRV	D0.1cc		< 40 Gy
Hippocampus_L or _R	D40% Dmean	< 7.3 Gy < 30 Gy	
SpinalCord_PRV	D0.1cc		< 40 Gy
Parotid_L or _R	D0.1cc	< 17 Gy	

1.7.4. 30 Gy in 6#

Maximum dose to lens < 6 Gy

Aim for maximum dose to all other outlined Organs at risk (eye, optic nerves, optic chiasm, and brainstem etc) < 100% of the prescribed dose i.e. 30 Gy

1.7.5. 34 Gy in 10#

Maximum dose to lens < 6 Gy

Aim for maximum dose to all other outlined Organs at risk (eye, optic nerves, optic chiasm, and brainstem etc) < 100% of the prescribed dose i.e. 34 Gy

1.8. Planning process/technique

IMRT/VMAT/conformal radiotherapy. For PTV:

Volume	Dose Required	Optimal Constraint	Mandatory Constraint
95%	>99%	x	
95%	>95%		x
2%	<105%	x	
0.1cc	<107%		x

1.9. Peer review

- All curative and adjuvant volumes should be prospectively peer reviewed before the start of treatment.
- A description of the contouring (planning note) and of the peer review process including changes made should be saved in the patient record.
- The peer review process and outcomes should be audited

1.10. Target verification

Modality	Frequency	Match point	Additional information
kV planar/ MV planar/CBCT/ MVCT	Daily IGRT	Automated bony match using a ROI placed around PTV. Radiographers should perform a visual check of structures. The match should be verified on all planes.	Consider use of low-dose CBCT or kV orthogonal imaging for benign tumours such as pituitary adenomas. For whole brain radiotherapy using parallel opposed technique a single 2D image may be sufficient.

1.11. Side effects

Possible early or short-term side effects	
Side effect	**Initial management (if appropriate)**
Tiredness	Provide a named healthcare professional with responsibility for coordinating health and social care support for people with brain tumours and their relatives and carers, for example, a key worker
Hair thinning or loss	Wig
Skin changes including soreness, itching or colour changes	Topical Emollient
Headaches	Soluble paracetamol/ co-codamol Morphine/ oxycodone Dexamethasone+ PPI
Loss of appetite	
Nausea or vomiting	Metoclopramide, ondansetron, domperidone, levomepromazine
Worsening of tumour-related symptoms	Steroids
Worsening or onset of seizures	Anticonvulsant medications
Changes to memory, concentration or slowing of thought	
Extreme sleepiness	
Effect on surgical wound which may delay healing or cause wound breakdown	
Changes in vision	
Dryness or soreness of the eye	
Changes in hearing which may include hearing loss, tinnitus or a feeling of fullness in the ear	Requiring regular syringing
Changes to balance, dizziness or co-ordination	
Hydrocephalus	Shunt

Possible late or long-term side effects	
Side effect	**Initial management (if appropriate)**
Permanent hair thinning or loss	Wig Finasteride for male baldness Minoxidil for female baldness
Changes to memory, concentration or slowing of thought which may be progressive and worsen time	Ongoing neuropsychology assessment for people at risk of cognitive decline. Neuro-cognitive rehabilitation Discuss health and social care support needs with the person with a brain tumour and their relatives and carers (as appropriate). Take into account the complex health and social care support needs people with any type of brain tumour and their relatives and carers may have (for example,

Possible late or long-term side effects	
	psychological, cognitive, physical, spiritual, emotional).
Radionecrosis	Corticosteroids
Stroke-like migraine attacks (SMART)	Corticosteroids
Worsening or onset of seizures	Anticonvulsant medications
Stroke or mini stroke	People who are at risk of stroke, consider checking their blood pressure, HbA1c level and cholesterol profile regularly. Refer to stroke services Neurorehabilitation
Brain, brainstem or spinal cord injury	
A benign tumour or different cancer in the treatment area	
Changes to pituitary hormone function	Consider refer to endocrinology team Consider checking their endocrine function regularly after the end of treatment once yearly TSH, FT4, FT3, IGF1, Cortisol, GH May require hormone replacement
Dryness of the eye	
Development of cataracts	Consider referring people who are at risk of visual impairment for an ophthalmological assessment. Operation if applicable
Change or loss of vision	
Changes in hearing	
Changes to balance, dizziness or co-ordination	

1.12. Follow Up

1.12.1. Follow up for glioma

Regular clinical review: standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume). CT brain with IV pre- and post-contrast if MRI is contradicted.

If findings from standard imaging are unclear about whether there is recurrence and early identification is potentially clinically useful, then consider advanced MRI techniques, such as MR perfusion, diffusion tensor imaging and MR spectroscopy.

Grade of tumour	Clinical review schedule
Grade 1 glioma	Scan at 12 months, then: • consider discharge if no tumour visible on imaging unless completely resected pilocytic astrocytoma • consider ongoing imaging at increasing intervals for 15 years for completely resected pilocytic astrocytoma • consider if ongoing imaging is needed at a rate of once every 1 to 3 years for the rest of the person's life if the tumour is visible on imaging
Grade 2 glioma **Grade 3 oligodendroglioma, 1p/19q codeleted**	• From 0 to 2 years, scan at 3 months, then every 6 months • From 2 to 4 years, review annually • From 5 to 10 years, review every 1 to 2 years • For more than 10 years and for the rest of life consider ongoing imaging every 1 to 2 years
Grade 3 astrocytoma **Grade 4 including glioblastoma**	• From 0 to 2 years, scan every 3 months • From 2 to 4 years, review every 6 to 12 months • From 5 to 10 years, review annually • For more than 10 years and for the rest of life consider ongoing imaging every 1 to 2 years

1.12.2. Follow up for meningioma

Regular clinical review: standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume). CT brain with IV pre- and post-contrast if MRI is contradicted.

	Grade 1: no residual tumour	Grade 1: residual tumour	Grade 1: after radiotherapy	Grade 2	Grade 3
0 to 1 years	Scan at 3 months	Scan at 3 months	Scan 6 months after radiotherapy	Scan at 3 months, then 6 to 12 months later	Every 3 to 6 months
1 to 2 years	Annually	Annually	Annually	Annually	Every 3 to 6 months
2 to 3 years	Annually	Annually	Annually	Annually	Every 6 to 12 months

3 to 4 years	Once every 2 years	Annually	Once every 2 years	Annually	Every 6 to 12 months
4 to 5 years	Once every 2 years	Annually	Once every 2 years	Annually	Every 6 to 12 months
5 to 6 years	Once every 2 years	Once every 2 years	Once every 2 years	Once every 2 years	Annually
6 to 7 years	Once every 2 years	Once every 2 years	Once every 2 years	Once every 2 years	Annually
7 to 8 years	Once every 2 years	Once every 2 years	Once every 2 years	Once every 2 years	Annually
8 to 9 years	Once every 2 years	Once every 2 years	Once every 2 years	Once every 2 years	Annually
>9 years (for the rest of life)	Consider discharge	Consider discharge	Consider discharge	Consider discharge	Annually

2. Brain metastases

In the management of confirmed brain metastases, the following factors should be taken into consideration:

- extracranial disease
- leptomeningeal disease
- location of metastases
- resection cavity size
- the number and volume of metastases
- the person's preference
- their age
- their performance status
- the primary tumour site, type, and molecular profile

2.1. Whole brain radiotherapy (WBRT)

WBRT can stabilise or reduce the brain metastases. It should not be offered with concurrent systemic therapy to enhance the efficacy of WBRT unless as part of a clinical trial.

2.1.1. Indications

- Multiple brain metastases or leptomeningeal disease
- Brain metastases that are not suitable for surgery or SRS
- For people with multiple brain metastases who have not had stereotactic radiosurgery/radiotherapy or surgery, decide with them whether to use whole brain radiotherapy after a discussion with them and their relatives and carers (as appropriate) of the potential benefits and risks
- Prophylactic Cranial Irradiation (PCI) for patients with small cell lung cancer

2.1.2. Exclusions

- Karnofsky performance status of under 70
- Factor in the patient's life expectancy and burden of extracranial disease

2.2. External beam post-operative cavity radiotherapy

2.2.1. Indications

- Incomplete resection as defined by surgeon or on review of postoperative imaging
- Piecemeal resection of the tumour as opposed to en-bloc resection
- Incision of cystic metastasis as part of debulking (leads to a higher chance of a contaminated bed and leptomeningeal dissemination)

2.2.2. Essential pre-radiotherapy investigations

- Bloods: FBC, U&E, LFTs for patients that require IV contrast imaging studies (planning CT / MRI)
- Planning MRI with pre- and post-contrast T1W, T2W and/or T2/FLAIR sequences

2.2.3. Localisation

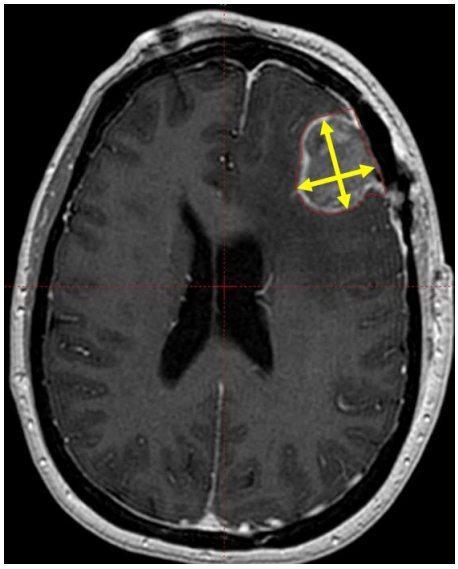
Localisation	Options	Notes
Position	Cranial	Patients should be positioned supine with their chin in a neutral position
Contrast	Cranial	No IV contrast unless planning MRI with contrast is contraindicated
Immobilisation	Cranial	5-point shell
CT acquisition	Slice thickness	1-3 mm
	Scanning limits	Up to C3
MRI brain protocol		Axial FLAIR, 3 mm, whole brain Axial T1+Gad, 3 mm, whole brain Sagittal T1, 3 mm, whole brain

2.2.4. Dose and fractionation

Determining the mean axial diameter of the cavity

The protocol stratifies dose regimen according to the size of the cavity. As the cavity can be an eccentric shape, please measure the mean axial diameter as follows:

- Find the slice on the scan where the cavity is largest. Usually this will be near the mid-point of the cavity in the superior-inferior dimension
- Measure the longest diameter, excluding the dural surface which is often bigger than the cavity itself.
- Measure a second diameter at right angles to the longest diameter
- Take the average of these two as a guide. See the image below as an example:



The following guidance should be used for dose and fractionation. Where possible, the CNS team will attempt to provide guidance on fractionation regimen in the MDT outcome. Please measure the mean axial diameter of the cavity and stratify fractionation as follows:

Mean axial diameter	Dose and fractionation	Estimated GTV	Estimated PTV	EQD2
32 mm	24 Gy in 3 fractions over 5 days	17 cc	44 cc	60 Gy
54 mm	30 Gy in 5 fractions over 10 days	82 cc	150 cc	60 Gy
86 mm or whole posterior fossa RT	30 Gy in 10 fractions over 12 days	333 cc	492 cc	37.5 Gy

Please ask the neuro-oncology team for advice if the cavity has a diameter of more than 86 mm

2.2.5. Target volumes

Use standard nomenclature as per AAPM 263[6].

GTV: should be the enhancing edge of the cavity and the entire dural surface that is adjacent to the cavity. There will be dural enhancement that extends away from the cavity where the dura has been opened.

CTV: should be grown by 2 mm and constrained to the inner surface of the skull bone. If you are planning PORT without MR imaging then a 5 mm CTV margin should be used. In addition, if the original metastasis was in contact with the dura, consider using 5 mm along the plane of the dura (discuss with neuro-oncology team).

PTV: 3-5 mm (refer to local policy)

2.2.6. Organs at risk

To help the planners, please segment the globes, lenses and brainstem as a minimum number of organs at risk. If the cavity is near the plane of the optic pathway, please contour the optics and chiasm.

Use standard nomenclature as per the Global Harmonization Group consensus guidelines[10]. See section 1.6 for further guidance on OAR delineation.

2.2.7. Dose constraints

2.2.7.1. 24 Gy in 3#

OAR	Optimal	Mandatory
Globes	16 Gy	None
Lenses	6 Gy	None
Optics and chiasm PRV	18 Gy	24 Gy
Brainstem PRV	18 Gy	24 Gy

2.2.7.2. 30 Gy in 5#

OAR	Optimal	Mandatory
Globes	20 Gy	None
Lenses	6 Gy	None

Optics and chiasm PRV	24 Gy	30 Gy
Brainstem PRV	24 Gy	30 Gy

2.2.7.3. 30 Gy in 10#

OAR	Optimal	Mandatory
Globes	26 Gy	None
Lenses	6 Gy	None
Optics and chiasm PRV	27 Gy	30 Gy
Brainstem PRV	27 Gy	30 Gy

2.2.8. Peer review

Volumes should be prospectively peer reviewed before the start of treatment. Any cases which do not match planning constraints, please liaise with the neuro-oncology team, and the neuro-oncology team will review and approve plans in the weekly planning meeting.

2.2.9. Target verification

Modality	Frequency	Match point	Additional information
kV planar / CBCT/ MVCT	Daily IGRT	Bone match to PTV	

2.2.10. Side Effects

Possible early or short-term side effects	
Side effect	**Initial management (if appropriate)**
Tiredness	Provide a named healthcare professional with responsibility for coordinating health and social care support for people with brain tumours and their relatives and carers, for example, a key worker
Hair thinning or loss	Wig
Skin changes including soreness, itching or colour changes	Topical Emollient
Headaches	Soluble paracetamol/ co-codamol Morphine/ oxycodone Dexamethasone+ PPI
Loss of appetite	
Nausea or vomiting	Metoclopramide, ondansetron, domperidone, levomepromazine
Worsening of tumour-related symptoms	Steroids
Worsening or onset of seizures	Anticonvulsant medications
Changes to memory, concentration or slowing of thought	
Extreme sleepiness	
Effect on surgical wound which may delay healing or cause wound breakdown	

Possible early or short-term side effects	
Changes in vision	
Dryness or soreness of the eye	
Changes in hearing which may include hearing loss, tinnitus or a feeling of fullness in the ear	Requiring regular syringing
Changes to balance, dizziness or co-ordination	
Hydrocephalus	Shunt

Possible late or long-term side effects	
Side effect	**Initial management (if appropriate)**
Permanent hair thinning or loss	Wig Finasteride for male baldness Minoxidil for female baldness
Changes to memory, concentration or slowing of thought which may be progressive and worsen time	Ongoing neuropsychology assessment for people at risk of cognitive decline. Neuro-cognitive rehabilitation Discuss health and social care support needs with the person with a brain tumour and their relatives and carers (as appropriate). Take into account the complex health and social care support needs people with any type of brain tumour and their relatives and carers may have (for example, psychological, cognitive, physical, spiritual, emotional).
Radionecrosis	Corticosteroids
Stroke-like migraine attacks (SMART)	Corticosteroids
Worsening or onset of seizures	
Stroke or mini stroke	People who are at risk of stroke, consider checking their blood pressure, HbA1c level and cholesterol profile regularly. Refer to stroke services Neurorehabilitation
Brain, brainstem or spinal cord injury	
A benign tumour or different cancer in the treatment area	
Changes to pituitary hormone function	Consider refer to endocrinology team Consider checking their endocrine function regularly after the end of treatment once yearly TSH, FT4, FT3, IGF1, Cortisol, GH May require hormone replacement
Dryness of the eye	
Development of cataracts	Consider referring people who are at risk of visual impairment for an ophthalmological assessment. Operation if applicable

Possible late or long-term side effects	
Change or loss of vision	
Changes in hearing	
Changes to balance, dizziness or co-ordination	

2.3. Follow up

Regular clinical review: standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume). CT brain with IV pre- and post-contrast if MRI is contradicted.

If findings from standard imaging are unclear about whether there is recurrence and early identification is potentially clinically useful, then consider advanced MRI techniques, such as MR perfusion, diffusion tensor imaging and MR spectroscopy.

Years after end of the treatment	Clinical review schedule
0 to 1 years	Every 3 months
1 to 2 years	Every 6 months
2 years onwards	Annually

2.4. Stereotactic radiosurgery (SRS)

These cases require discussion at the neuro-oncology MDT which should include up-to-date staging of extra-cranial disease and an indication of prognosis/treatment options from the referrer. The commissioning criteria require that patients must have:

- KPS 70 or above
- Controllable extra-cranial disease
- Absence of pressure symptoms that would be best relieved by surgery
- Tumour volume of no more than 20 cc
- Life expectancy from extra-cranial disease expected to be greater than 6 months

Individualised considerations are required for patients with new lesions in the context of previous SRS, or re-treatment of previously treated lesions.

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5. Amendment History

A record of changes in this document

Date	Updated version number	Previous version number	Page Number/ Section (updated version)	Details
29.12.21	V1.0			New Document
05.01.22	V1.1	V1.0	31	NSCLC removed as contraindication for WBRT
06.02.23	V2.0	V1.1	5.0	Section on OARs updated to include GHG consensus guidelines as per Network Oversight Group request
13.05.24	V3.0	V2.0	Throughout	Formatting changed to align with network documents
			4.1	Updated GBM CTV margin to 15 mm (ESTRO-EANO 2023)
			10.1	Added follow-up scheduled for scan every 3 months in first 2 years of GBM/high grade astrocytoma follow-up
				Side effect sections updated utilising RCR consent forms
28.08.25	V3.1	V3.0	1.1	Clarified wording for GBM in unmethylated >70 Added note about PBT consideration for medulloblastoma Formatting and copy editing changes which do not significantly change content but aid in consistency, readability and deduplication within the document Meningioma added to indications
			1.4	Added 59.4 Gy / 33# as an option for G2 astrocytoma Used 59.4 Gy / 33# for all G3 glioma Removed 50 Gy / 30# as an option for G2 meningioma
			1.5.2	Updated LGG CTV margin to 10 mm (ESTRO-EANO 2025)
			1.6 and 1.7	Updated a few structure names in line with GHG consensus guidelines Added pituitary to OAR structure list Updated description of lacrimal gland
			1.7.1	Brainstem_PRV constraint updated

			1.11 and 2.2.10	Added steroids for the management of SMART syndrome and RN
			2.2.2	Removed DWI sequences from essential pre-radiotherapy investigations for cavity PORT