East of England Radiotherapy Network Central Nervous System Protocol

Contents

I. Primary Brain Tumours

1.0 Indications and patient population

1.1 Inclusion criteria

A. Radical radiotherapy and concomitant chemotherapy post-operatively/ biopsy – for all suitable patients with high grade gliomas (WHO grade III and IV)

A.1 Radical Radiotherapy and concomitant+/- chemotherapy post-operatively/biopsy-for all suitable patients with Grade Gliomas IV

A.1.1 Radical radiotherapy using 60 Gy in 30 fractions with concomitant temozolomide, followed by up to 6 cycles of adjuvant temozolomide, for people aged around 70 or under who have:

- A Karnofsky performance status of 70 or more and
- Had maximal safe resection, or biopsy when resection is not possible, for a newly diagnosed grade IV glioma (glioblastoma).

A1.2 Radical radiotherapy using 40 Gy in 15 fractions with concomitant and up to 12 cycles of adjuvant temozolomide for people aged around 70 or over who have:

- A Karnofsky performance status of 70 or more and
- A newly diagnosed grade IV glioma (glioblastoma) with MGMT methylation.

A1.3 For patients not covered of the above criteria:

- Radiotherapy alone using 60 Gy in 30 fractions
- Hypofractionated Radiotherapy using 40 Gy in 15 fractions or 30Gy in 6 fractions
- Hypofractionated Radiotherapy using 40 Gy in 15 fractions+/- TMZ for patients aged <70 with borderline fitness for Stupp protocol
- Up to 6 cycles of temozolomide alone if the tumour has MGMT methylation and the person is aged around 70 or over.

A2 Radical Radiotherapy and concomitant+/- chemotherapy post-operatively/biopsy-for all suitable patients with Grade Gliomas III with or without 1p19q co-deletion

A2.1 Sequential radical radiotherapy and 4 to 6 cycles of PCV chemotherapy to people who have:

- A Karnofsky performance status of 70 or more and
- A newly diagnosed grade III glioma with 1p/19q co-deletion

(anaplastic oligodendroglioma).

A2.2 Radical radiotherapy followed by up to 12 cycles of adjuvant temozolomide to people who have:

- A Karnofsky performance status of 70 or more and
- A newly diagnosed IDH-wildtype or mutated grade III glioma without 1p/19q co-deletion (anaplastic astrocytoma).

B Radical Radiotherapy for Low Grade Gliomas II with evidence of progression of neurological symptoms, uncontrolled seizures, larger tumours, older age group>40 years old, IDH negative, 1p19q non –codeleted

B1 After surgery, offer radiotherapy followed by up to 6 cycles of PCV chemotherapy (procarbazine, CCNU [lomustine] and vincristine) for people who:

- Have a 1p/19q codeleted, IDH-mutated low-grade glioma (oligodendroglioma) and
- Are aged around 40 or over or have residual tumour on postoperative MRI.

B2 After surgery, consider radiotherapy followed by up to 6 cycles of PCV chemotherapy for people who:

- Have a 1p/19q non-codeleted, IDH-mutated low-grade glioma (astrocytoma) and
- Are aged around 40 or over or have residual tumour on postoperative MRI.
- Patients may be offered Temozolomide instead of PCV (outside of NICE guidelines). Patients need to be fully consented if MDT agrees.

Be aware that the prognosis for people with histologically confirmed IDH-wildtype grade II glioma may be similar to that of people with glioblastoma if other molecular features are consistent with glioblastoma. Take this into account when thinking about management options.

C Re-irradiation for Glioma with localized disease recurrence after first- or second-line chemotherapy

Be aware of the Combs Criteria: WHO Grade III or IV, Age>50 yrs., Time from initial radiation to re-irradiation >12 months, KPS<80, No re-resection, Size <47cc

D Radical Radiotherapy for Diffuse Grade II Ependymoma and Anaplastic Ependymoma Grade III

D.1 Radical Radiotherapy for Grade I meningiomas when incomplete excision (Simpson 4 to 5) or no excision (radiological diagnosis only)

D.2 Adjuvant/Radical Radiotherapy for inoperable Grade II meningiomas when excision (Simpson 1 to 5) or no excision(radiological diagnosis only)

D.3 Adjuvant/Radical Radiotherapy for inoperable Grade III meningiomas when excision (Simpson 1 to 5) or no excision(radiological diagnosis only)

E Adjuvant/Radical Radiotherapy for Haemangioperitomas

F Curative radiotherapy/Adjuvant Radiotherapy for Pituitary and Craniopharyngiomas (e.g. residual tumour or tumour progression post-surgery, invasion of cavernous sinuses, uncontrolled hormones levels)

G Adjuvant Radiotherapy for Medulloblastoma, Germinoma and Pineoblastoma

H Radical radiotherapy for Vestibular Schwannoma for patients not eligible for surgery

I Paraganglioma (Glomus tumours) for patients not eligible for surgery

J Radical /Palliative Radiotherapy for Chordomas/ Chondrosarcomas for skull base, spinal and sacral for patients not eligible for Proton Treatment (e.g. metal implants)

K Radical /Adjuvant treatment for Spinal cord Tumours with incomplete excision

L Palliative Radiotherapy for High Grade Gliomas Grade III and IV

1.2 Exclusion criteria

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

1.3 Essential Pre-Radiotherapy investigations for curative patients

- Bloods – FBC, plus U&E, LFTs for the patients that require iv contrast for CT or who have received concomitant or sequential 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

2.0 Localisation

Localisation	Notes	
Position	Cranial	Patients should be positioned supine with their chin in a neutral position
	Cranial –Skull base	Supine in a neutral position
	Spinal- Cervical Lesions	Supine, thermoplastic mask, head straight in a neutral position
	Spinal- Thoracic lesions	Supine, consider chest pole, with arms raised
	Spinal-Lumbar/Sacral Lesions	Supine with knee rest and ankle stocks
	Spinal	If patient in pain-prone position might be helpful
Arm/ leg/ head/ thorax position	Cranial	Arms down
	Spinal	Arms down-Arms up (thoracic)
Immobilisation and supports	Cranial	Thermoplastic beam direction shell with either 5- or 9-point fixation
	Cranial –Skull base	High precision mask fixation system
	Spinal	Thermoplastic mask
Organ pre-requisites	N/A	No preparation acquired
Contrast	Cranial	iv contrast
CT acquisition	Slice thickness:	1-3mm
	Scanning limits for Cranial Lesions	Up to C3
	Scanning limits for Skull base	Generally 1–2 mm thickness from the vertex to the bottom of the third cervical vertebra (C3)

MRI Brain protocol	High grade planning	Axial T2 Axial, 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 FLAIR, 3 mm, whole brain
		Axial T2 Axial, 3 mm, whole brain
		Axial T1+Gad, 3 mm, whole brain
	Tumours within or close to optic pathways	Axial T2 Axial, 3 mm, whole brain
		Axial T1+Gad, 1 mm, whole brain
		Axial LAVA Flex 1mm slices
	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 slices 3D Geometric correction enabled Axial Reformat of 3D FLAIR

3.0 Dose prescription & chemotherapy

Intent	Dose (Gy)/#	#/week	Chemo/ comments
Radical Radiotherapy and concomitant+/- chemotherapy post-operatively/biopsy-for all suitable patients with Grade IV Gliomas (Cranial)	60/30	5/week	Concomitant temozolomide 75mg 75 mg/m2 daily seven days a week /6-12 cycles of adjuvant temozolomide at 150-200mg/m2 given 5 days in every 28 (Age <70, PS 0-1, KPS 70-100)
	40/15	5/week	Concomitant temozolomide 75mg/m2 daily seven days a week during RT then 6-12 cycles of adjuvant temozolomide at 150-200mg/m2 given 5 days in every 28 Can also consider treatment with temozolomide if MGMT+ve and > 70. If MGMT-ve then no temozolomide (Age >70 PS 0-1, KPS 70-100)
Radical Radiotherapy and concomitant +/- chemotherapy post-operatively/biopsy-for all suitable patients with Grade III Gliomas with or without 1p19q co-deletion	59.4/33	5/week	Non-codeleted (anaplastic astrocytoma) 1p19q followed by 12 cycles of TMZ. Then up to 12 cycles of adjuvant temozolomide at 150-200mg/m2 given 5 days in every 28 days
	60/30	5/week	High Grade III Glioma with concomitant TMZ. Then up to 6 cycles of adjuvant temozolomide at 150-200mg/m2 given 5 days in every 28 (treated as a GBM)
	60/30	5/week	High Grade III Glioma
	54 /30	5/week	Co-deleted (anaplastic oligodendroglioma) 1p19q followed by 4-6 cycles of PCV
	50.4/30		

Palliative High Grade (III and IV) glioma RT	30/6	3/week	High Grade Gliomas (Grade III and IV)
	34/10	5/week	High Grade Gliomas (Grade III and IV)
Radical Radiotherapy for Low Grade II Gliomas with evidence of progression of neurological symptoms, uncontrolled seizures, larger tumours, older age group>40 years –old, IDH negative, 1p19q non –codeleted	54 /30 50.4/28	5/week	Co-deleted (oligodendroglioma) 1p19q followed by 4-6 cycles of PCV
Radical Radiotherapy for Low Grade II Gliomas with evidence of progression of neurological symptoms, uncontrolled seizures, larger tumours, older age group>40 years –old, IDH negative, 1p19q non –co-deleted	54 /30 50.4/30	5/week	Astrocytoma Grade II followed by up to 6 cycles of PCV. Patients may be offered Temozolomide instead of PCV (outside of NICE guidelines). Patients need to be fully consented if MDT agrees.
Re-irradiation for Glioma with localized disease recurrence after first- or second-line chemotherapy	36/12 35/10	5/week	Combs Criteria: WHO Grade III or IV Time from initial radiation to re-irradiation 12 months KPS>80 No re-resection Size<47cc (Combs Criteria) Consider 35 Gy in 10 fractions for GTV greater than 47cc

Radical Radiotherapy for Diffuse Grade II Ependymoma and Anaplastic Grade III Ependymoma	54/30	5/week	Grade II diffuse- can be observed post-operatively if they had complete removal
	59.4/33	5/week	Grade III
Radical Radiotherapy for Grade I meningioma	50/30	5/week	Consider radiotherapy where there is likely to be residual disease remaining after surgery e.g. adjacent to critical structures. Take into consideration the consequences of a recurrence and the ease of reoperation.
	50.4/28	5/week	Radical RT for unresectable meningiomas
	54//30	5/week	Radical RT for unresectable meningiomas
	55/33	5/week	Radical RT for unresectable meningiomas
Radical Radiotherapy for Grade II meningioma	50/30 54/30 55/33 60/30	5/week	Radiotherapy can be indicated after complete resection as these lesions are at higher risk of recurrence
Radical Radiotherapy for Grade III meningioma	60/30	5/week	Adjuvant is indicated
Curative radiotherapy/Adjuvant Radiotherapy for Pituitary: • extensive post-operative residual tumour • invasion of cavernous	45/25	5/week	Pituitary as standard dose
	50/30		Very large or invasive tumours
	55/33		Pituitary Carcinoma

sinuses • uncontrolled hormones levels • tumour progression after the operation	54/27-30		Pituitary as standard dose
Curative radiotherapy/Adjuvant Radiotherapy for Grade I Craniopharyngiomas	50/30	5/week	Standard dose
	55/33		Aggressive tumour(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 50-52.2Gy*
	54/28		Standard dose
	52.2/27		Standard dose
Medulloblastoma	36/20	5/week	Followed by boost RT to primary site and any focal spinal metastases as followed:
Cranial boost	19.8/11	5/week	Whole posterior cranial fossa for metastatic medulloblastoma
Spinal boost Diffuse Spinal cord metastasis	3.6/2	2/week	
Medulloblastoma with diffuse leptomeningeal disease	39.6/22 14.4/8	5/week	*With diffuse leptomeningeal disease whole CSA dose to 39.6Gy in 22 fractions, with the tumour bed boost then 14.4Gy in 8 fractions*
Focal spinal cord boost	9/5	5/week	Above the termination of the spinal cord
	14.4/8		Below the termination of the spinal cord
Germinoma	40/24	5/week	Delivered in two phases: Phase1 - CSA 25Gy / 15 # Phase2 - Boost 15Gy / 9 #

Pineoblastoma	55/33	5/week	Delivered in two phases: Ph1 - CSA 35Gy / 21 # Phase2 - Boost 20Gy / 12#
Vestibular schwannoma	12/1	5/week	Consider 12 Gy in 1 fraction with SRS. Fractionated RT: The aim of the treatment is to control / stabilise growth not remove the tumour so active FU post RT is required.
	50/30		
Glomus Tumours (paraganglioma)	50/30	5/week	Radiotherapy has the advantage of very low toxicity, but the disadvantages that the tumour remains and the very low risk of second tumours.
Chondrosarcomas for skull base, spinal and sacral for patients not eligible for Proton Treatment (e.g. metal implants)	65-70/39	5/week	The aim of the treatment is to control / stabilise growth.
Spinal Cord Tumours	50/30	5/week	Ependymoma and astrocytoma histology
	55/33		
	50.4-54/30		Glioblastoma
	54-60/30		Cauda equine glioblastoma
	50/30		Meningioma, schwannoma

4.0 Target volumes

- Use standard nomenclature as per AAPM 263
- https://www.aapm.org/pubs/reports/RPT_263.pdf

4.1 Radical radiotherapy GTV/CTV

Radical Radiotherapy and concomitant chemotherapy post-operatively/biopsy-for all suitable High Grade III and IV Gliomas

MRI produces superior definition of tumour, and the T1-weighted with gadolinium (T1W+Gd) and T2/FLAIR sequences should be co-registered to the planning CT.

GTV: The gross tumour (GTV) is defined as the visible contrast-enhancing edge of tumour, shown most clearly on MRI, using T1W with gadolinium contrast. According to the EORTC protocol, the GTV is defined as the surgical resection cavity plus the residual enhancing tumour or as unresected enhancing tumour defined by T1W+Gd. The post surgical changes (infarction or gliosis) should be taken under consideration. A comparison of planning MRI with preoperative scans and postoperative diffusion-weighted imaging (DWI) can help differentiate post-op vascular changes from residual tumour.

For example, patients with secondary GBM (IDH mutant), non-enhancing areas may be a component of the tumour; in such cases, consideration may be given to include hyperintensity on T2/FLAIR in the GTV in addition to the contrast enhancing tumour, because the high signal regions are considered to represent regions of low-grade tumour.

CTV : GVT+2cm (ESTRO-ACROP protocol). CTV does not have to extend beyond the inner table of the skull, which is best shown on CT using the bone window. Ideally, the CTV should be edited to account for natural barriers such as ventricles (5mm), falx (5mm), and tentorium cerebelli (5mm). The CTV crosses the midline when the tumour extends to the contralateral hemisphere or infiltrates the corpus callosum.

Radical Radiotherapy and chemotherapy for all suitable High-Grade II Gliomas

4.1.2 Radical Radiotherapy for Low Grade II Gliomas with evidence of progression of neurological symptoms, uncontrolled seizures, larger tumours, older age group >40 years – old, IDH negative, 1p19q non –co-deleted

GTV: should be delineated as the full extent of visible abnormality demonstrated on the T2W or FLAIR MRI. For patients who underwent a surgery, GTV should include the post-operative residual disease and the surgical cavity.

CTV: CTV = GTV + 1.5cm (1.0-2.0)

This should be grown using the automatic 3D growing algorithm and then care should be taken to restrict the CTV to anatomically plausible areas of tumour spread including editing to the inner edge of the skull.

Re-irradiation of gliomas

GTV: This should be delineated as the extent of visible abnormality as demonstrated on the T1W + Gd MRI. 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 0.5 - 1 cm.

Ependymomas

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

Posterior Fossa tumours:

GTV: GTV represents any residual post-operative tumour as demonstrated on T1W +Gd MRI.

CTV: post-operative cavity allowing 1.0-2.0 cm for all low-and high-grade. Consider the whole posterior fossa as CTV.

Supratentorial tumours

GTV: define the GTV as any residual post -operative enhancing tumour in MRI T1W+Gd.

CTV: GTV+ 1.5–2.5 cm (dependent on grade), grown isotropically, which can be edited along the skull.

Meningiomas:

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.

GTV: The gross tumour (GTV) is defined as the area of abnormality or any residual tumour and the resection cavity (if available) as demonstrated on the T1W + Gd post op MRI sequence, without inclusion of the perilesional oedema. Also, the 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.

Whether resection has been carried out, co-registration with the preoperative MRI is immensely helpful in order to delineate pre-operative GTV. **Pre-operative GTV** shows the

location of the tumour and therefore the meningeal surfaces into which spread might occur, ensuring that the meningeal tail of the tumour, as well as the nodular enhancement is defined.

In addition, the hyperostotic bone; only directly invaded bone and clearly hyperostotic bone should be included in the GTV using a CT bone window setting to improve target delineation.

CTV: There is little hard evidence for the size of the CTV margin that should be used. For an individual tumour, its growth pattern suggests whether a small or large margin is needed whether there is brain invasion or bony erosion

Use the pre-op imaging to show the 'base' of the lesion and ensure that this area is included. The CTV margin is based on a combination of histology and growth pattern, as follows:

Grade 1 : CTV = GTV

Grade 2 : along the meninges CTV = GTV + 0.5cm - 1cm and at other surfaces CTV = GTV

Grade 3 : along the meninges CTV = GTV + 1-2 cm, should include the pre-operative tumour bed, peritumoural oedema, hyperostotic bone changes and dural enhancements or thickening and CTV = GTV + 0.5-1 around natural barriers to tumour growth, such as the skull base and into surrounding brain parenchyma unless there is evidence of invasion.

Pituitary and Craniopharyngioma

Pituitary

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 cranio – 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.

Vestibular Schwannoma

GTV: the enhancing lesion as demonstrated on T1W MRI with contrast enhancement and fast imaging employing steady sate acquisition (FIESTA) may be useful for improving the visualization of the cisternal segments of cranial nerves. In addition, bony CT windows are helpful since the enlargement of vestibular canal can be visible representing the tumour volume
CTV=GTV

Germinoma

Phase 1 should treat craniospinal axis, and this is most effectively planned from CT.
Phase 2, GTV : is the contrast-enhancing tumour in MRI T1W

CTV: 1–2 cm, grown isotropically

Medulloblastoma in adults

Phase 1 :should treat 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 1.5 cm.

Paragangliomas (Glomus Tumour)

GTV: the enhancing lesion as demonstrated on T1W + Gd MR sequence

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

Chordomas and Chordosarcomas

GTV: the enhancing lesion as demonstrated on T1W + Gd and/or T2W MR 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.

Spinal Cord Tumours

GTV: includes the residual tumour visible on the T1 enhancing abnormality on MRI or the tumour onT2/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 1.5 cm for low grade tumours, and 2-3 cm 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+2 cm proximally and distally

PTV:

1. For radical treatments: PTV:CTV+3-5mm

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

5.0 Organs at risk

- Aim for the use of standard nomenclature as per Global Harmonization Group consensus guidelines:

  https://www.thegreenjournal.com/action/showPdf?pii=S0167-8140%2820%2930294-2

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.
Lacrimal Gland	The T2-precontrast and T1-weighted images are preferred for delineation. LG lies in the supero-lateral (medially to the zygomatic process of the frontal bone) Extraconal portion of the orbit. Located superior to the lateral rectus muscle and lateral to the superior rectus muscle.
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.
Optic Nerve PRV	A Planning Risk Volume (PRV) is created to account for positioning error using an appropriate margin, usually 2-3mm 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.
Optic Chiasm _PRV	A Planning Risk Volume (PRV) is created to account for positioning error using an appropriate margin, usually 2-3mm.
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.
Hippocampi	T1-weighted MRI or use the PD T2-weighted MRI. MRI slices along the axis of the hippocampus allows better visualization. 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.

5.1 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.

5.1a 60Gy in 30#

Structure name	Constraint	Optimal	Mandatory
Brainstem (PRV)	D0.1cc	<54Gy	59 Gy (V59Gy<10cc)
Lens_L or _R	D0.1cc	< 6 Gy	< 10Gy
Eye_L or _R	D0.1cc	<40Gy	
Cornea	D0.1cc	30Gy	
Cochlea_L or _R	Dmean	<40Gy to ipsilateral cochlea & <10Gy to contralateral cochlea (COSTAR)	
Lacrimal Gland	D0.1cc	< 26Gy	
Optic Nerve (PRV)	D0.1cc	< 50 Gy	< 54-55Gy to whole structure
Optic Chiasm (PRV)	D0.1cc	< 50Gy	< 54-55Gy to whole structure
Pituitary	D0.1cc	<45 Gy to whole gland	
Spinal Cord (PRV)	D0.1cc	< 48Gy	< 50 Gy
Parotid_L or _R	Dmean	< 20Gy	
Temporal Lobe	V60Gy	<5.5 cc	
Mandible Bone	D0.1cc	<50 Gy	<60 Gy
Hippocampi	D40% Dmean	<7.3 Gy < 30 Gy	

5.1b 50Gy in 30#

Structure name	Constraint	Optimal	Mandatory
Brainstem (PRV)	D0.1cc	< 48Gy	< 51.5Gy
Lens_L or _R	D0.1cc	< 6Gy	< 10Gy
Eye_L or _R	D0.1cc	< 40Gy	
Cornea	D0.1cc	< 30Gy	
Cochlea _L or _R	Dmean	Mean dose <40Gy to ipsilateral cochlea and <10Gy to contralateral cochlea (COSTAR)	
Lacrimal Gland	D0.1cc V30 Gy	< 26Gy < 50%	
Optic Nerve (PRV)	D0.1cc	< 48 Gy	< 51.5 Gy
Optic Chiasm (PRV)	D0.1cc	< 48Gy	< 51.5Gy
Pituitary	D0.1cc	<45 Gy	
Spinal Cord (PRV)	D0.1cc	<48Gy	< 51.5 Gy
Parotid_L or _R	Dmean	< 20Gy	
Mandible Bone	D0.1cc	< 50 Gy	
Hippocampi	D 40% Dmean	<7.3 Gy < 30 Gy	

5.1c 40Gy in15#

Maximum dose to lens <4Gy

Maximum dose to all other outlined Organs at risk (eye , optic nerves, optic chiasm, and brain stem etc. < 100% of the prescribed dose e.g. 40Gy)

Maximum plan dose < 105% of the prescribed dose e.g. 42Gy

Structure name	Constraint	Optimal	Mandatory
Brainstem (PRV)	D0.1cc		<40 Gy
Lens_L or _R	D0.1cc		< 4Gy
Eye_L or _R	D0.1cc	<40Gy	
Cornea	D0.1cc	<30Gy	
Cochlea_L or _R	D mean	<39 Gy	
Lacrimal Gland	D0.1cc	<22Gy	
Optic Nerve (PRV)	D0.1cc		<40 Gy
Optic Chiasm (PRV)	D0.1cc		<40 Gy
Hippocampi	D40% Dmean	<7.3 Gy < 30 Gy	
Spinal Cord (PRV)	D0.1cc		<40 Gy
Parotid_L or _R	D0.1cc	<17 Gy	

5.1d 30Gy in 6#

Maximum dose to lens <6Gy

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

5.1e 34Gy in 10#

Maximum dose to lens <6Gy

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

6.0 Planning process/ technique

- IMRT/VMAT/conformal
- PTV Coverage:

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

If mandatory constraints are not met (i.e. significant overlap of PTV/ OAR), aim for a CTV coverage of V100%≥95%.

7.0 Peer Review/ Contour QA

- 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

8. 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.

9.0 Side effects

9.1 Possible early or short-term side-effects	
Side effect	**Management (if appropriate)**
Skin erythema	Topical Emollient
Hair Loss	Wig
Headaches	Soluble paracetamol/ co-codamol Morphine/ oxycodone Dexamethasone+ PPI
Nausea	Metoclopramide, ondansetron, domperidone, levomepromazine
seizures	Anticonvulsant medications
Irritation of treated ear canal	1- 6 weeks post RT – olive oil drops / micro-suction preferable
Fatigue & lethargy	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
Thickening of ear wax on treated side	Requiring regular syringing

9.2 Possible late or long-term side effects	
Side effect	**Management (if appropriate)**
Pituitary dysfunction	Require hormone replacement therapy
Decreased cognitive function- including memory loss/ effects of cognition	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

9.2 Possible late or long-term side effects	
	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).
Risk of cataract formation	Consider referring people who are at risk of visual impairment for an ophthalmological assessment. Operation if applicable
Risk of damage to the optic apparatus-visual deterioration	Consider referring people who are at risk of visual impairment for an ophthalmological assessment assessment and treatment for risk factors e.g. diabetes
Low risk of permanent hair loss in the treatment area	Wig Finasteride for male baldness Minoxidil for female baldness
Risk of stroke	People who are at risk of stroke, consider checking their blood pressure, HbA1c level and cholesterol profile regularly. Refer to stroke services Neurorehabilitation
Risk of cranial nerve effects	Consider referring people who are present with cranial nerves effects to neurology team for assessment
Hypopituitarism	Consider refer to endocrinology team Consider checking their endocrine function regularly after the end of treatment once yearly TSH, FT4,FT3,IG1,Cortizol, GH May require hormone replacement
Risk of second tumours	N/A

10.0 Follow up

10.1. Follow up for Gliomas Grade I-IV

Scans:

1. 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
2. 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

Clinical review schedule for patients with glioma depending on Grade of tumour

Grade of tumour	Clinical review schedule
Grade I	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 II 1p/19q noncodeleted, IDH mutated Grade II 1p/19q codeleted Grade III 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 II IDH wildtype Grade III 1p/19q noncodeleted Grade IV (glioblastoma)	• 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.

10.2. Follow up for Meningioma

Scans:

1. 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.

Clinical review schedule for patients with meningioma depending on Grade of tumour

	Grade I: no residual tumour	Grade I: residual tumour	Grade I: after radiotherapy	Grade II	Grade III
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

II .Brain Metastasis (BM)

Management of confirmed brain metastasis we need to consider:

- ✓ 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.

1.0 Indications for Whole brain Radiotherapy (WBRT)

Whole brain Radiotherapy (WBRT)

1.1 Indications:

1. Can stabilise or reduce the brain metastases
2. 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
3. Prophylactic Cranial Radiotherapy for patients with small cell lung cancer
4. Do not offer concurrent systemic therapy to enhance the efficacy of whole-brain radiotherapy to people with multiple brain metastases, unless as part of a clinical trial

1.2 Contradictions of WBRT:

1. Brain metastases that are not suitable for surgery or stereotactic radiosurgery/radiotherapy
2. Karnofsky performance status of under 70.

2.0 External Beam post-operative cavity radiotherapy

1. Incomplete resection as define by surgeon or review in post-operative imaging
2. Piece meal resection of the tumour as opposed to en –bloc resection

3. Incision of cystic metastasis as part of debulking, which lead to higher chance of a contaminated bed and leptomeningeal dissemination of diseases

2.1 Essential Pre-Radiotherapy investigations for treated patients

- cranial MRI with pre- and post-contrast T1-weighted,
- T2-weighted and/or T2-fluid-attenuated inversion recovery (FLAIR)
- a diffusion-weighted imaging (DWI) sequences [EANO III, C; ESMO IV,B].

2.2 Localisation

Localisation	Notes	
Position	Cranial	Patients should be positioned supine with their chin in a neutral position
Contrast	Cranial	No IV contrast, unless patient have an implant or pacemaker (not suitable for MRI scan) then with iv contrast
Immobilization	Cranial	5-point shell
CT acquisition	Slice thickness:	1-3mm
	Scanning limits	Up to C3
MRI Brain protocol		Axial FLAIR, 3mm, whole brain
		Axial T1+Gad, 3 mm, whole brain
		Sagittal T1, 3 mm, whole brain

2.3 Determination of the cavity

Determining the mean axial diameter of the cavity

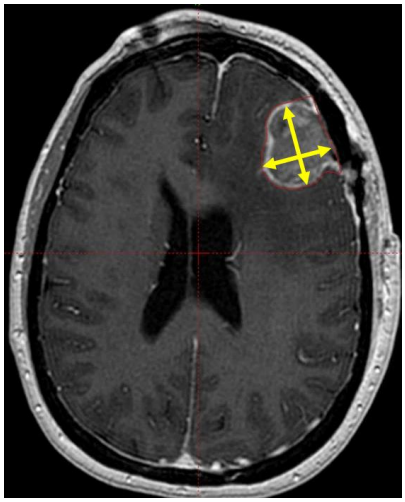
The protocol stratifies dose regimen according to the size of the cavity. As the cavity can be an eccentric shape, please measure the mean axial diameter as follows:

•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:



3.0 Dose and fractionation

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
32mm	24Gy in 3 fractions over 5 days	17cc	44cc	60Gy
54mm	30Gy in 5 fractions over 10 days	82cc	150cc	60Gy
86mm or whole posterior fossa RT	30Gy in 10 fractions over 12 days	333cc	492cc	37.5Gy

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

4.0 Target volumes

5. Use standard nomenclature as per AAPM 263
6. https://www.aapm.org/pubs/reports/RPT_263.pdf

- 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 2mm and constrained to the inner surface of the skull bone. If you are planning PORT without MR imaging then a 5mm CTV margin should be used.
  In addition, if the original metastasis was in contact with the dura, consider using a 5mm along the plane of the dura (discuss with neuro-oncology team).
- PTV : 3-5 mm.
  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.

5.0 Organs at risk

- **See section 5.0 for I. Primary Brain Tumours**
- Aim for the use of standard nomenclature as per Global Harmonization Group consensus guidelines:
  https://www.thegreenjournal.com/action/showPdf?pii=S0167-8140%2820%2930294-2

5.1 Dose Constraints

5.1a 24Gy in 3#

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

5.1b 30Gy in 5#

OAR	Optimal	Mandatory
Globes	20Gy	None
Lenses	6Gy	None
Optics and chiasm PRV	24Gy	30Gy
Brainstem PRV	24Gy	30Gy

5.1c 30Gy in 10#

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

6.0 Peer Review/ Contour QA

- 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.

7.0 Target verification

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

8.0 Side Effects

8.1 Possible early or short-term side effects	
Side effect	**Management advised (if appropriate)**
Skin erythema	Topical Emollient
Hair Loss	Wig
Headaches	Soluble paracetamol/ co-codamol Dexamethasone (low dose up to 4mg)+PPI (lansoprazole, omeprazole)
Nausea	Metoclopramide, ondansetron, domperidone, levomepromazine
seizures	Anticonvulsant medications

9.0 Follow up

Scans:

1. 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

2. 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.

Possible regular clinical review schedule for people with brain metastases

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

10.0 Stereotactic Brain radiotherapy

MDT discussion.

Referral to appropriate centre.

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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13.0 Amendment History

A record of changes to 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