Thames Valley and Wessex Radiotherapy Operational Delivery Network (ODN)

Radiotherapy Protocols

Intracranial Stereotactic Radiosurgery/ Radiotherapy

This document is the standardised Thames Valley and Wessex Radiotherapy Network Adult Primary CNS Tumours (including benign) treatment protocol developed collaboratively by the ODN SRS/SRT Protocol Working Group:

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Document History

Date of Issue	Version Number	Date Approved	Responsible for Change	Nature of Change	Ratification/ Approval
08.09.2021	V 0.1 (1st draft)		The SRS Working Group	Aligning existing local protocols and existing published evidence	
20.10.2021	V 0.2 (2nd draft)		The SRS Working Group	Minor amendments	
24.11.2021	V 0.3 (3rd draft)		The SRS Working Group		
09.02.2022	V 1.0 (final)		The SRS Working Group		
14.12.23	V 2.0		The SRS Working Group	Protocol review and update in line with the latest clinical evidence	Thames Valley and Wessex RT NOG

Contents

Primary Objective and Scope

To summarise the planning and treatment of adult patients receiving intracranial stereotactic radiosurgery/ radiotherapy for use in Radiotherapy Centres in the Thames Valley and Wessex Radiotherapy Network.

Indications

Exclusion Criteria

1. Patient inability to provide informed consent or comply with the treatment requirements.
2. Patient inability to undergo MRI imaging is a relative contraindication, depending on the quality of CT scans available.
3. Patients who otherwise do not meet the inclusion criteria outlined below.

Inclusion Criteria

Vestibular Schwannoma (VS) (Acoustic Neuroma) other cranial nerve schwannomas/neuromas

Indications:

- Newly diagnosed as an alternative to surgery
- Residual disease after microsurgery
- Recurrent disease after surgery
- Intracanalicular tumours if tumour growth is documented after observation.
- Histological verification is not required.
- SRS may be used where the tumour is less than 3 cm in extra-canalicular diameter AND there are no clinical signs of brainstem compression.If the shape of the tumour is a narrow cylinder, the maximum tumour dimension may be up to 5cm.

Outcome:

- Compared with surgery, SRS gives similar levels of tumour control (95% at 5 years and 93% at 10 years), with better levels of facial nerve (95%) and hearing preservation (70% at 10 years), a less detrimental impact on quality of life and lower rates of procedural mortality and medium-term treatment related complications.
- Patients aged ≤ 60 years and those with tumours ≤1.5cm3 may have better facial nerve preservation with SRS than those over 60 and with larger lesions.
- Note that 30% may show transient increase between 6- and 30-months post SRS before shrinking. Up to 10% may develop hydrocephalus.
- 3% of patients treated will require subsequent surgical resection.
- Note that in some SRT series (e.g. 25Gy in 5 fractions) disease control is 82% and hearing preservation 30% .

Skull base glomus tumours and paragangliomata

Indication:

- SRS may be used where the tumour is less than 3 cm diameter where surgery is contraindicated or relative risks of surgery are high, or for recurrence <3cm following surgery.

Meningioma

Indication and technique:

WHO Grade 1

- Symptomatic/critical sites, where resection is not possible.
- >0.3cm to optic chiasm / nerve
- <3cm diameter
- <13cm^3
- Adjacent to brainstem AND there are no clinical signs of brainstem compression or located on the convexity of the skull
- small recurrence following fractionated radiotherapy
- incompletely resected small volume disease
- NB Histological verification is not required if radiology is certain.

fSRT is indicated in WHO Grade 1 meningioma not meeting the above criteria and all WHO Grade 2/3 meningioma.

WHO Grade 2/3 Meningioma

Small volume recurrence following previous surgery or radiotherapy.

Outcome:

- WHO Grade I meningioma: >90% tumour control at 5 and 10 years following SRS approx. 30% reduction in size (not usually significant reduction)

Pituitary Adenoma

Indication and technique:

- SRS may be used for primary disease or for small volume symptomatic (including secreting) pituitary recurrence following surgery and or conventional RT /fSRT
- >0.3cm from the optic chiasm
- Tumour volume <4cm^3.

Outcome:

- 10 year control rate is in the region of 90 – 95% for SRS
- Biochemical disease control 44% at 6 years for SRS (GH secreting)
- Fractionated radiotherapy to pituitary adenomas is associated with

- 1-2% risk of radiation optic neuropathy
- 20-30% risk of developing pituitary hormone deficiency requiring replacement therapy
- 4 fold increase in relative risk of CVA.

CNS Metastases

Indication:

- **Initial treatment of metastases:**

The role of single fraction SRS in the primary treatment of CNS metastases is considered particularly useful for patients whose brain metastases are of small volume and surgically inaccessible, or with high risk of new deficit after surgery.

- Patients must have a Karnofsky Performance Status (KPS) ≥ 70 (WHO PS ≤ 2)
- The diagnosis of cancer must be established and there must be absent or controllable primary / metastatic disease. CT CAP wtihin 4 weeks prior to decision to treat with SRS.
- The tumour site MDT has confirmed that the patient's life expectancy from any treatable extra-cranial primary or metastatic disease is expected to be greater than 6 months.
- Pressure symptoms which would be best relieved by surgery are excluded.
- Pre-treatment scans must not show a total tumour volume of more than $20cm^3$. This will usually mean that no individual tumour has a diameter in excess of 3cm. Multiple lesions totalling up to $20cm^3$ may be treated.
- Patients should be treated within 2 weeks of decision to treat in clinic.

- **Recurrent treatment of metastases with SRS/SRT:**

- SRS/SRT may be used to treat new lesions in patients where SRS/SRT has previously been effective, provided:
- A period of **three** months has elapsed since the last SRS/SRT treatment
- AND the above criteria (for initial treatment of metastases) are all met
- AND the disease specific cancer MDT has reviewed the patient and confirmed the appropriateness of further SRS/SRT.

- Repeat treatment of lesions previously treated with SRS/SRT or WBRT will only be supported if:
- A period of six months has elapsed since the last SRS/SRT/WBRT treatment
- AND criteria above (for initial treatment of metastases) are all met
- AND the disease specific cancer MDT has reviewed the patient and confirmed the appropriateness of further SRS/SRT.

- SRS may be used to treat the tumour bed for incompletely resected metastases as shown on immediate post op MRI or for recurrence of resected metastases following an MRI at any stage post-surgery if the above criteria for SRS are met.

Technique:

- SRS may be used for lesions total volume <20cm^3 (~3cm maximum diameter; which are not in critical locations: i.e. brainstem, basal ganglia or internal capsule.
- SRT (3-5 fractions) is used for metastases total volume <20cm^3 in critical locations such as in brainstem, adjacent to optic structures, basal ganglia or internal capsule OR if normal brain dose constraints are not met for single fraction technique.

Ependymoma, haemangioblastoma, pilocytic astrocytoma, trigeminal schwannoma

See (NHSE CCP- 16058/P)
https://www.england.nhs.uk/wp-content/uploads/2018/07/Stereotactic-radiosurgery-radiotherapy-for-epedymoma-haemangioblastoma-pilocytic-astrocytoma-and-trigeminal-sc.pdf

Contouring Guidelines for Primary CNS Tumours

The following target volumes and OARs will be segmented by the consultant oncologist and reviewed by a neuroradiologist. Additional review by a second oncologist is strongly recommended and these may also be reviewed by a neurosurgeon.

Tumour site	GTV	CTV (includes MRI fusion/contouring uncertainty)	PTV
Vestibular Schwannoma	Enhancing lesion on MRI (T1+contrast and FIESTA sequence) or CT if MRI contraindicated – see detailed guidelines below	GTV	CTV+0.1cm
Glomus skull base tumour	Enhancing lesion on MRI or CT if MRI contraindicated	GTV	CTV+0.1cm
Meningioma	Enhancing lesion on MRI or CT (if MRI contraindicated) + nodular dural tail + hyperostotic invaded bone	GTV	CTV +0.1cm
Pituitary PitNET	Microadenoma /recurrence as identified on MRI T1 with and without contrast, for secreting pituitary adenoma Methionine PET may be helpful.	GTV	CTV + 0.1cm

CNS metastases	Enhancing lesion or resection cavity on MRI or CT if MRI contraindicated	**Tumour:** GTV **Following resection:** GTV to encompass any enhancement and whole resection cavity adjacent to original tumour	GTV+0.1 – 0.2cm

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.

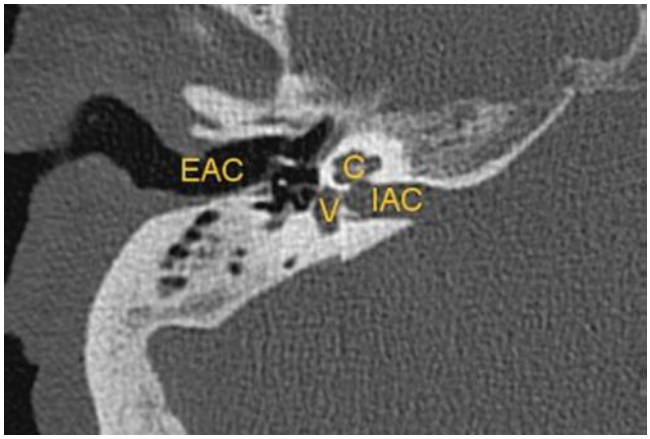

Figure 1. Axial CT through skull base. IAC, internal auditory canal, EAC, external auditory canal, C, cochlea, V, vestibule (Bhandare et al., 2010)

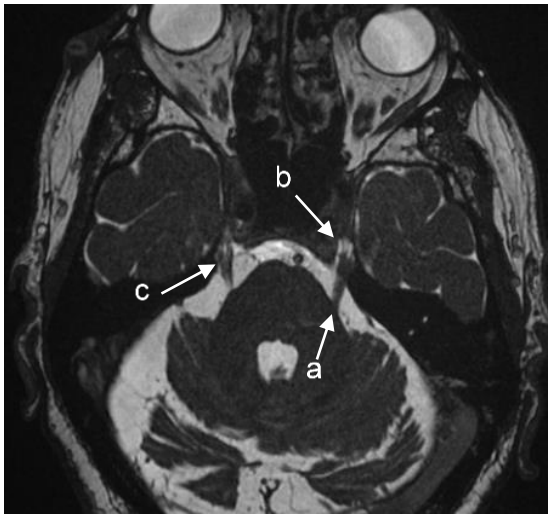

Figure 4. FIESTA sequence, 0.4 mm slices. The left trigeminal nerve is seen exiting the brainstem (a) and entering Meckel's cave (b). The right trigeminal nerve is also seen (c). (SRFT imaging).

Dose and Fractionation

Tumour site	Tumour size or GTV constraint	SRS	SRT
Vestibular Schwannoma/ Trigeminal schwannoma and other cranial nerve schwannomas	<3 cm diam (or up to 5cm if cylindrical in shape) AND No brainstem compression.	12 Gy to PTV	21Gy / 3 #
Glomus skull base tumour	<3 cm (or up to 5cm if cylindrical in shape) AND No brainstem compression	15Gy (as per RCR benign tumour 2015 guidelines)	No
Meningioma Grade 1 only (or unbiopsied)	<13cm^3 >0.3cm from optic nerve/chiasm	For tumours up to 4 cm^3 13-15Gy to PTV	For tumours up to 13 cm^3 21Gy / 3 #
Meningioma Grade 1 Retreatment following fSRT	Skull base <20cm^3 Non skull base <13cm^3	13-15 Gy	21Gy / 3 #
Meningioma Grade 1 Retreatment following SRS		13-15 Gy	21Gy / 3 #
Meningioma Grade 2-3 Retreatment following fSRT	Skull base <20cm^3 Non skull base <13cm^3	14-21 Gy	24Gy / 3 #

Pituitary PitNET – >0.3cm from chiasm/optic nerves or recurrence	Recurrence is < 4cm^3 AND >0.3cm from the optic chiasm	13-16 Gy to PTV for non-functioning adenomas. Consider up to 20Gy for functioning adenoma NB previous RT lower dose to PTV dep on chiasm dose	21-24Gy/3#
CNS metastases/ resection cavity NOT in critical location: brainstem, basal ganglia, internal capsule.	Total mets GTV <20cm^3	18-24 Gy to PTV * see below. Give highest dose to achieve Brain V12<8.5 cm^3 (optimal) V12< 10cm^3 (mandatory) Plus meet other OAR constraints. 15Gy could be considered following peer review discussion.	21, 24, 27Gy in 3# in 7, 8 or 9Gy per # used if Brain V12 is >10cm^3 for a single fraction
CNS metastases In critical locations such as: brainstem, basal ganglia, internal capsule, optic structures	GTV<20 cm^3	Generally not used but 15Gy could be considered following peer review discussion	25-30Gy to PTV in 5 x 5-6 Gy#
Pilocytic astrocytoma	<3 cm diameter	18-24Gy/1#	21, 24, 27Gy in 3# used if Brain V12 is >10cm^3 for a single fraction
Pineal	<3 cm diameter	18-24Gy/1#	21, 24, 27Gy in 3# used if Brain V12 is >10cm^3 for a single fraction
Haemangioblastoma	<3 cm diameter	18-24Gy/1#	21, 24, 27Gy in 3# used if Brain V12 is >10cm^3 for a single fraction
Ependymoma	<3 cm diameter	18-24Gy/1#	21, 24, 27Gy in 3# used if Brain V12 is >10cm^3 for a single fraction

Normal Tissue Dose Constraints

Planning risk volumes for Organs at Risk
PRV = OAR + 0.1cm margin (0.2cm if OAR is >5cm from isocentre)

^ *From UK 2022 Consensus on Normal Tissue Dose-Volume Constraints for Oligometastatic, Primary Lung and Hepatocellular Carcinoma Stereotactic Ablative Radiotherapy (Diez P, et al, Clinical Oncology 2022 34: 288-300)*
~ *From ESTRO ACROP guideline for target volume delineation of skull base tumors (Combs S, et al, Radiotherapy and Oncology 2021 156: 80-94)*

Tissue	constraint	1 fraction		3 fractions		5 fractions	
		optimal	mandatory	optimal	mandatory	optimal	mandatory
Note that Hotspots in OAR PRVs >107% should be avoided.							
Optic PRV ~	Dmax (<0.003cm^3)	<8Gy	<10Gy	<15Gy	<19.5Gy	<22.5 Gy	<25Gy
Brainstem PRV ^	Dmax (<0.03cm^3)	<12.5 Gy	<15Gy	<18Gy	<23.1Gy	<23Gy	<31Gy
Spinal cord PRV (including medulla)	Dmax (<0.003cm^3)	<12.4Gy ^	<14Gy ^	<18Gy	<20.3Gy ^	<23Gy	<25.3Gy ^
	D 1cm^3	<7Gy		<12.3Gy		<14.5Gy	
Normal brain (minus GTV)	V 12 Gy	<8.5cm^3	<10 cm^3		<50cm^3		
	V 18 Gy ~				<26cm^3		
	V 20 Gy						<30 cm^3
	D 50%	<5Gy					
Normal brain (minus GTV)	For multiple mets OUH use agreed calculation below: V12Gy1# + V19.6Gy3# + V24.4Gy5# < 30cm^3						
PTV coverage should NOT be compromised to meet the constraints shown below:							
Cochlea	Mean	<4Gy ^	<9Gy		<17.1Gy ^		<25Gy ^
Cochlea ~	Dmax (0.003cm^3)		Aim for lowest possible dose (eg 4Gy Dmax) BUT Dmax = 14 Gy <25% risk of hearing loss		20 Gy (<3%)		27.5 Gy (3%)
Lens	Dmax (0.003cm^3)	<1.5Gy ^		<5.2 Gy		<6 Gy	
Orbit	Dmax (0.003cm^3)	<8Gy ^		<16.2Gy		<20 Gy	
Skin ^	Dmax (0.1cm^3)		<26Gy	<33Gy		<39.5Gy	
Skin ^	D10cm^3		<23Gy	<30Gy		<36.5Gy	

Plan evaluation parameters for SRS/SRT plans:

- Prescription isodose should cover PTV but may be compromised to 95% and preferably 99% of PTV to receive prescription dose in order to meet PRV organ at risk dose constraints. GTV MUST be fully covered by prescription dose.
- PTV Dose max as local protocol
- Target coverage ratio: PTV V_{PD} (cc) / PTV volume (cc)
- Selectivity index: PTV V_{PD} (cc) / Body V_{PD} (cc)
- Paddick conformity index (PCI) = target coverage × selectivity
- Gradient index 1 (GI_1) = Body $V_{(50\% \text{ of PD})}$ (cc) / Body V_{PD} (cc)
- Record Gradient index 2 (GI_2) = Body $V_{(50\% \text{ of PD})}$ (cc) / PTV volume (cc)

Parameter	**Optimal**	**Mandatory**
Target coverage	≥ 0.98	≥ 0.95
Selectivity index	≥ 0.9	≥ 0.75
Paddick Conformity index	≥ 0.8	≥ 0.6
Gradient index1	< 3	< 5

Additional medication

Patients undergoing 1-5 fraction treatment should usually receive corticosteroids.

- For metastatic disease: Supportive medications such as dexamethasone and Ondansetron should be prescribed as per local protocol to start on the day of treatment and continued until the day after treatment has been completed, along with a proton pump inhibitor e.g. omeprazole 20mg PO od. This may be followed by a dose reduction as instructed by the clinician, usually reducing to 0mg over 4 days, but may be extended to 4-5 weeks for patients already taking steroids before SRS. If the patient is already on steroids, the dose should be increased as outlined above on these days.

- Steroids may not be required for benign lesions treated with SRS depending on level of oedema/proximity to brain/ brainstem.

- *A prophylactic course of anti-convulsant medication can be prescribed at the clinician's discretion.*

Appendix 1: 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