Clinical Target Volumes for Brain Tumors

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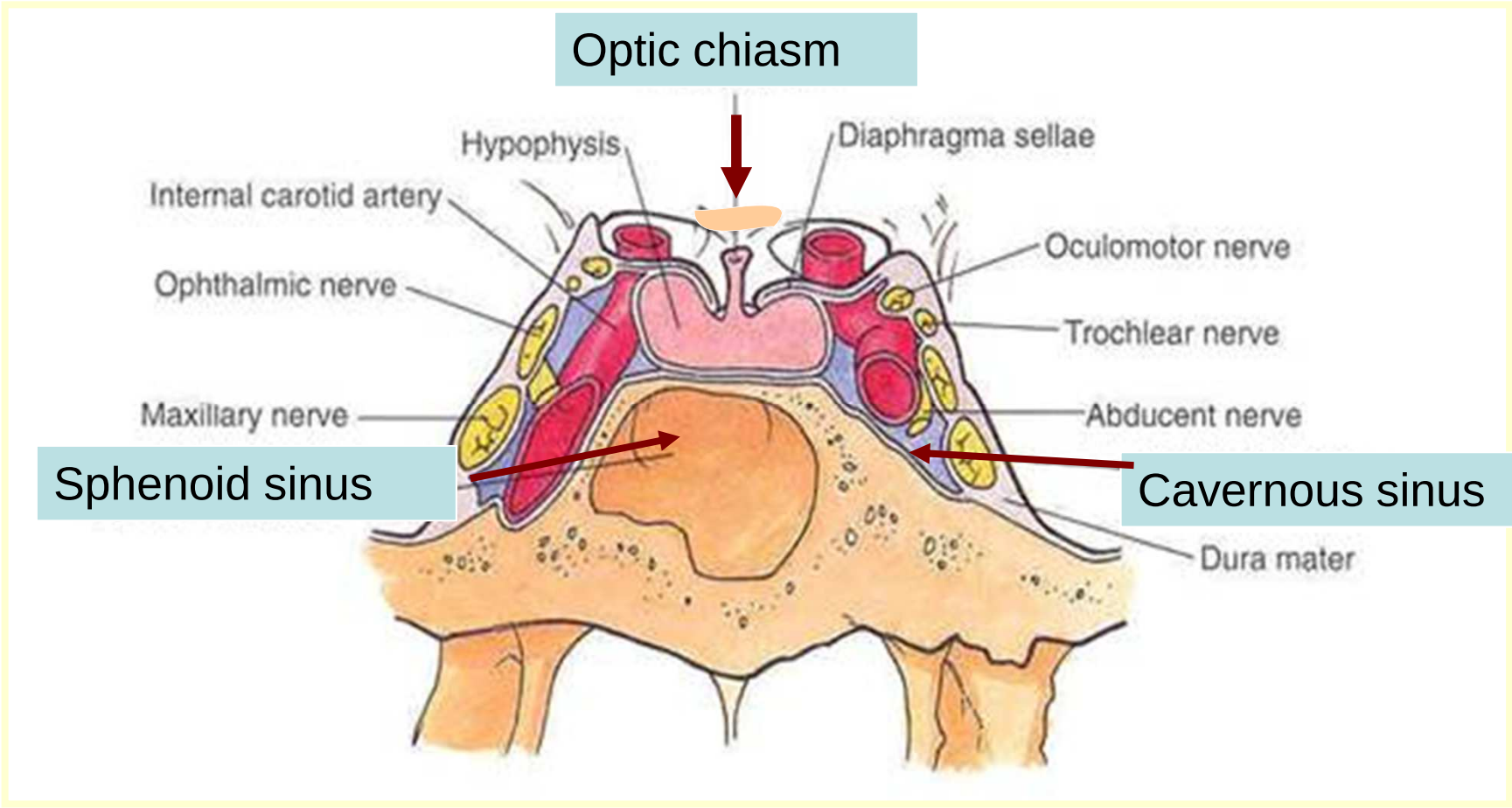
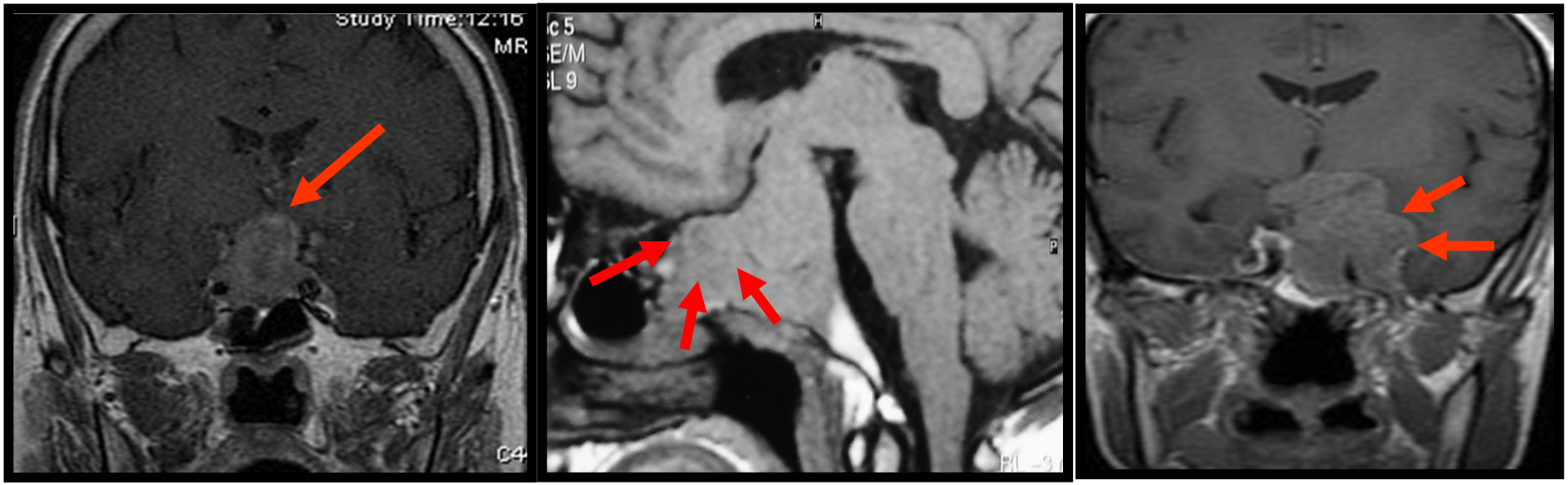
Benign brain tumors: Road map

- Presentation, natural history and reasons to treat
  - Pituitary adenomas
  - Craniopharyngiomas
  - Acoustic neuromas
  - Meningiomas (WHO Grade 1)
  - High grade Gliomas
  - Low grade gliomas
- The gross and clinical targets for each
- The PTV and to what doses

Pituitary: Anatomic relations



Pituitary: Patterns of growth & symptoms/signs

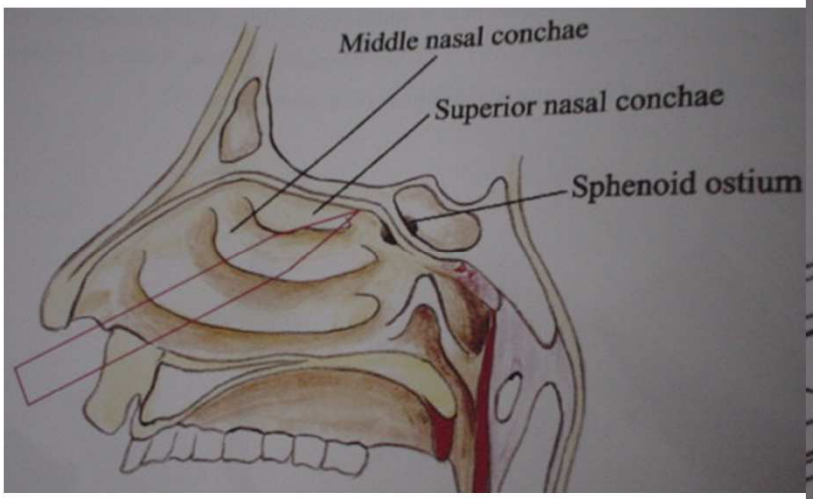


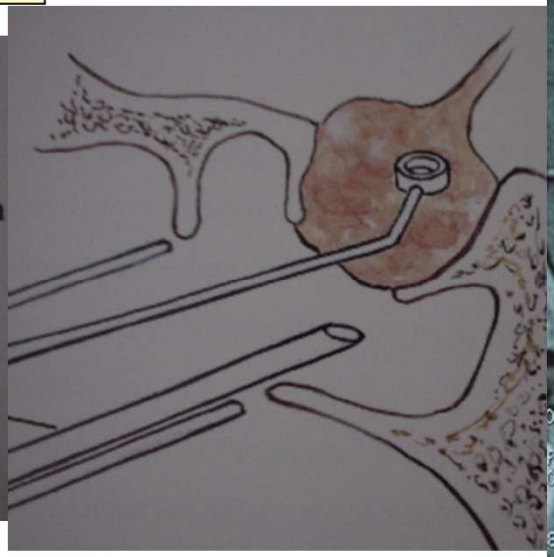
Headache, vomiting
Cranial Nerves: Vision, 3rd, 4th,5th & 6th
Amenorrhoea, galactorrhoea, acromegaly

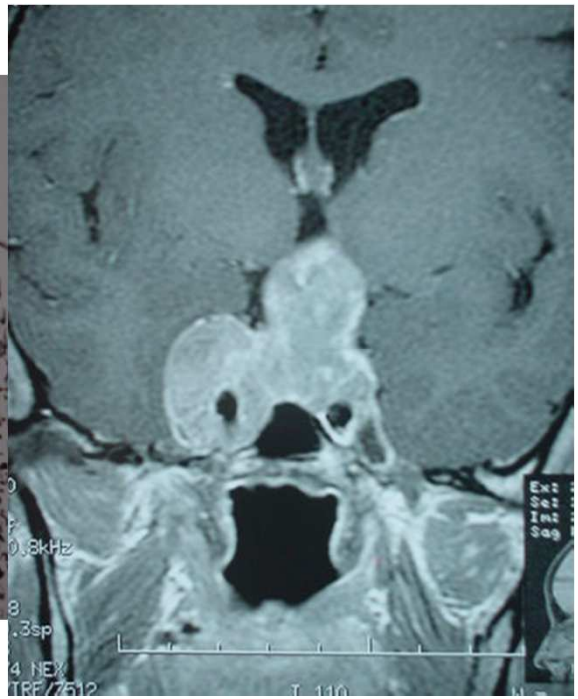
Pituitary: Surgical approach & Reasons to treat

Surgery
- **Non-functioning adenomas with mass effect**
- **Most secretory adenomas**

Medical therapy
Prolactinomas







Residual (cavernous sinus invasion or suprasellar)

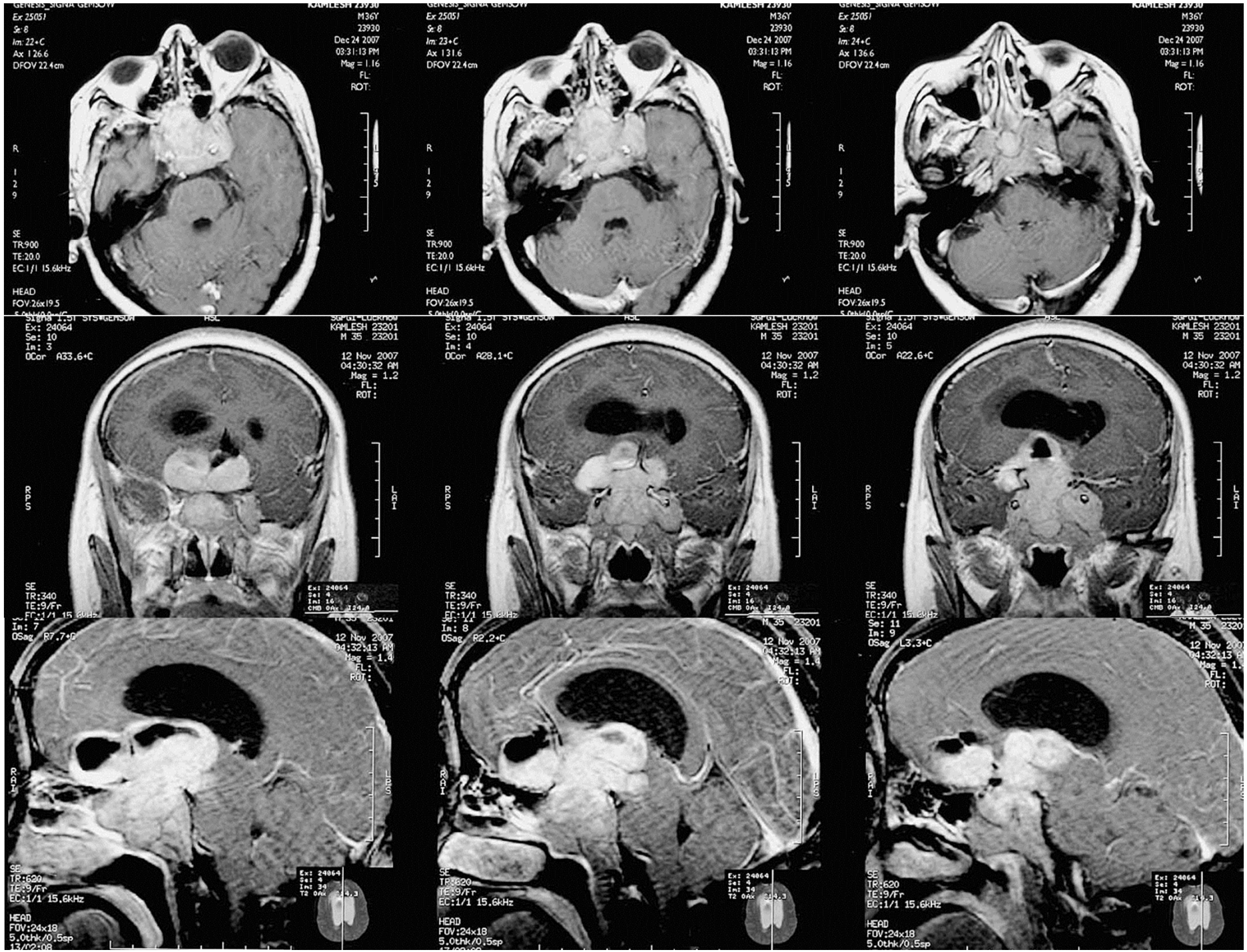
Recurrent (sometimes aggressive histology)

Persistently elevated hormonal levels (i.e. failure of normalization of GH, PRL or ACTH)

Trans-cranial approach for parasellar extension, ICA encasement

Pituitary: What to draw

- This is a BENIGN tumor. Takes several years to attain the size which calls attention (in non-functioning ones)
  - So, no hurry to treat a residual. It can be done 3-6months after surgery or at any time later
- Imaging needs:
  - The narrower, the better (2 mm for SCRT) say 3mm for conventional
  - Plain and ?contrast scans (Distinction with clivus is blurred, so avoided)
  - Study axial, sagittal and coronal scans on MRI to identify patterns of spread
  - Extension to sphenoid sinus can be real or more usually post surgical fat pad
  - If in doubt about involvement of an area, contour it!
  - So draw OBVIOUS residual and PRESUMED residual into one outline: Call it whatever you want GTV or CTV. No margins beyond obvious tumour are needed for a CTV
  - 3-5mm (or more) margin for PTV & 45Gy/25fx/5weeks for all types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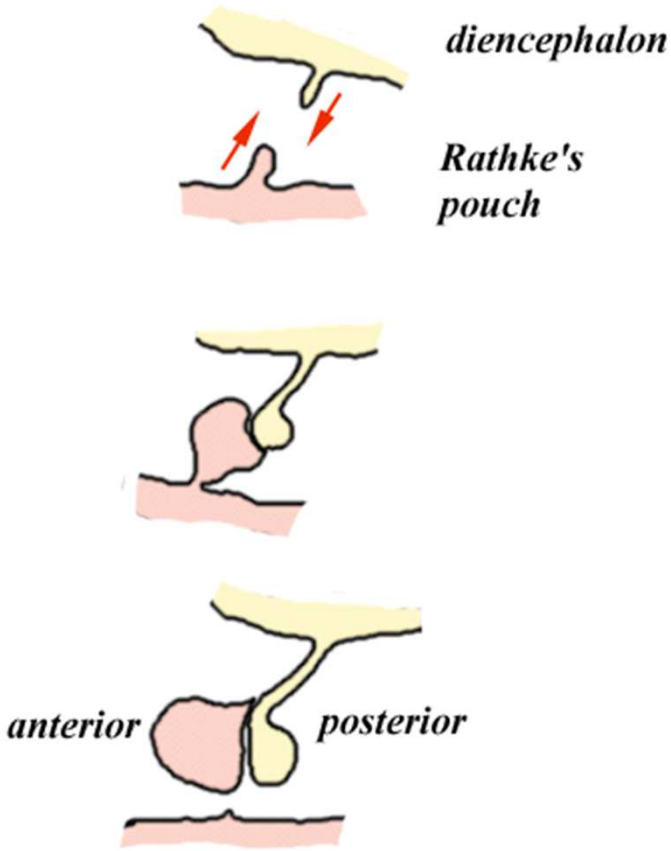
Craniopharyngioma

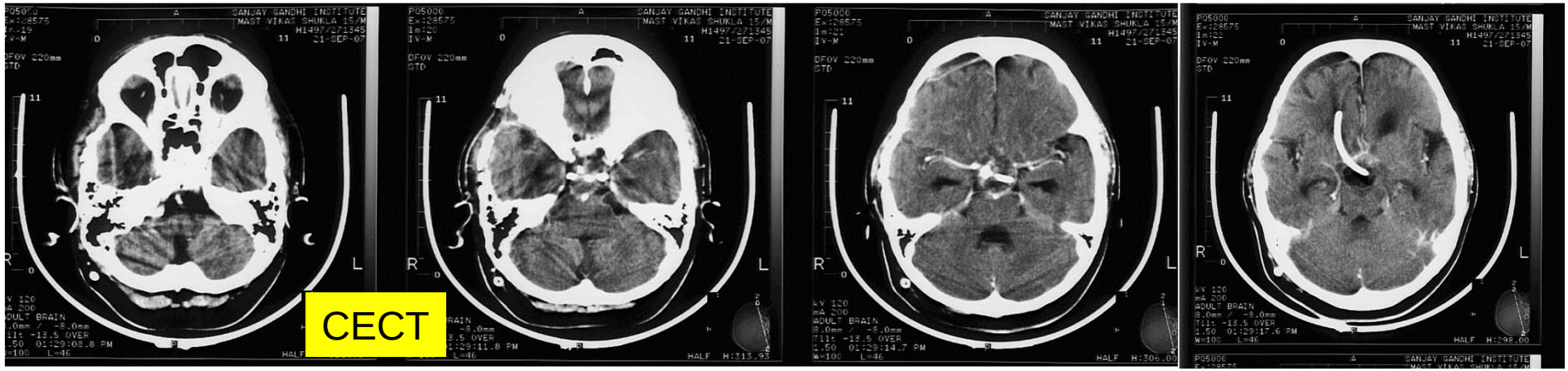
- Tumor arises from the remnant of Rathke's pouch in the supra-sellar area
- Usually cystic in children
- Headaches, visual problems and consequences of hypothalmic-pituitary damage
- Treatments:
  - Surgery (Biopsy, cyst drainage, partial removal or complete removal [mortality, morbidity, hypothalmic damage, visual deterioration, endocrine complications In 30-70%])
  - Partial excision + FSRT= 10yr FFP-75 to 85%



Craniopharyngioma: What to draw?

- Tumor has proximity and propensity to invade with ‘finger like’ projections surrounding structures, i.e. pituitary & hypothalamus
- Use narrow slices, 2-3 mm and combination of plain and contrast CECT and T1-w (plain and with Gd) MRI in multiple planes
- See both pre-op and post op imaging
- GTV = visible residual lesion including solid and cystic components
- CTV = GTV (known microscopic extension is not considered a predictor of recurrence
- GTV (CTV) to PTV expansion 5 – 10 mm depending upon technology
- Dose= 50Gy in 30 -33 fx (1.51-1.67 Gy/fx as proportion are children)

Minniti et al, Radiother Oncol 82:90-95, 2007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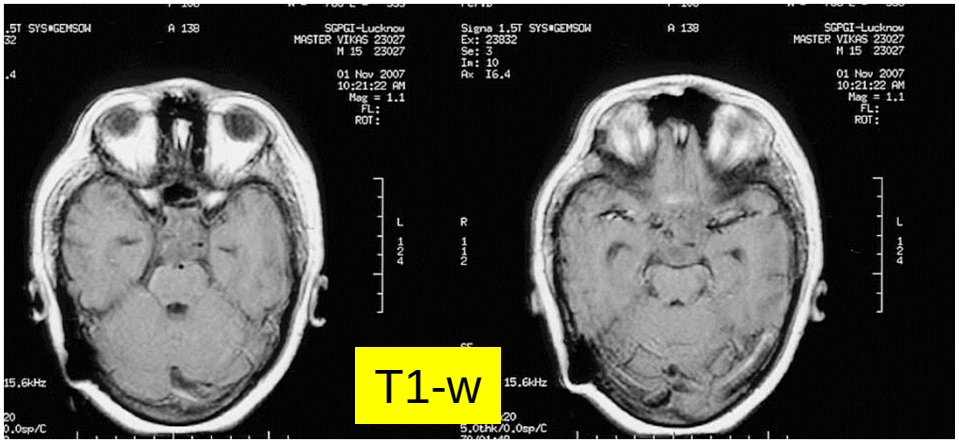
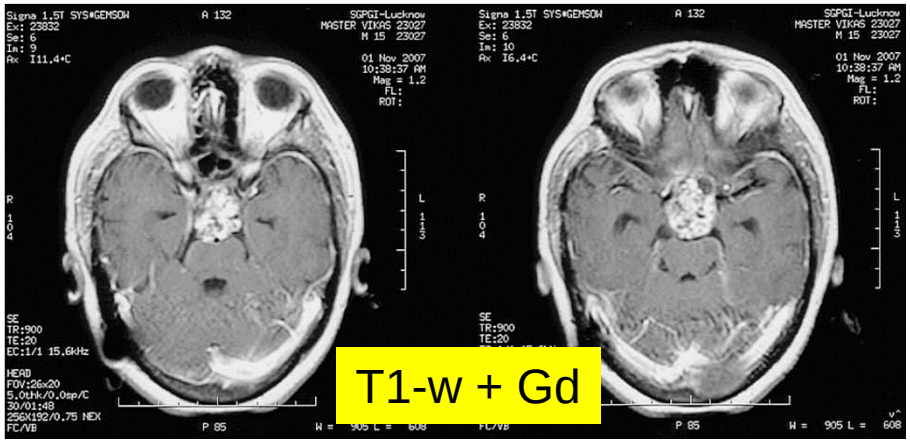
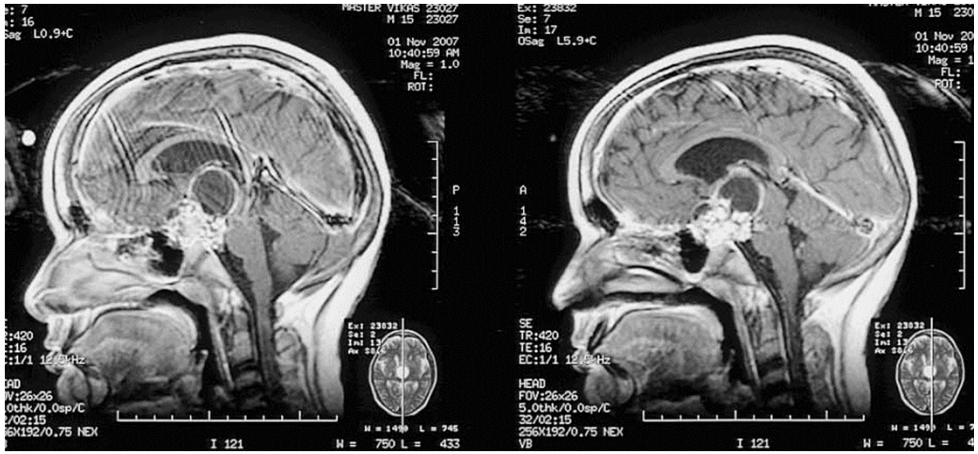
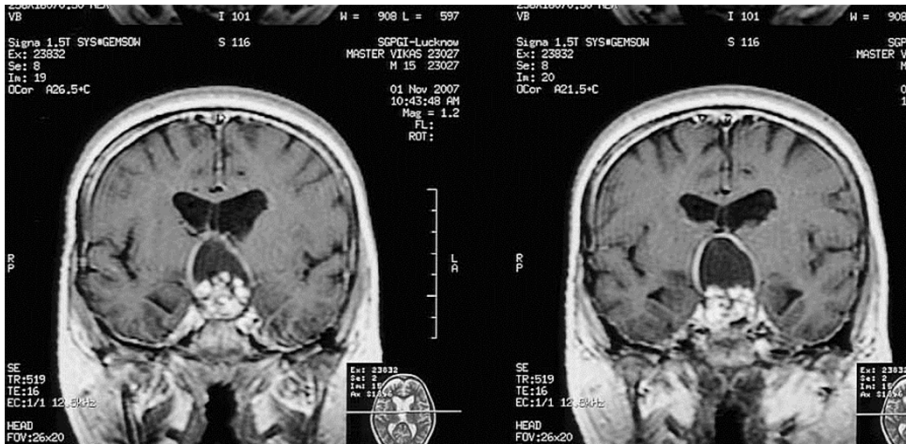

T1-w

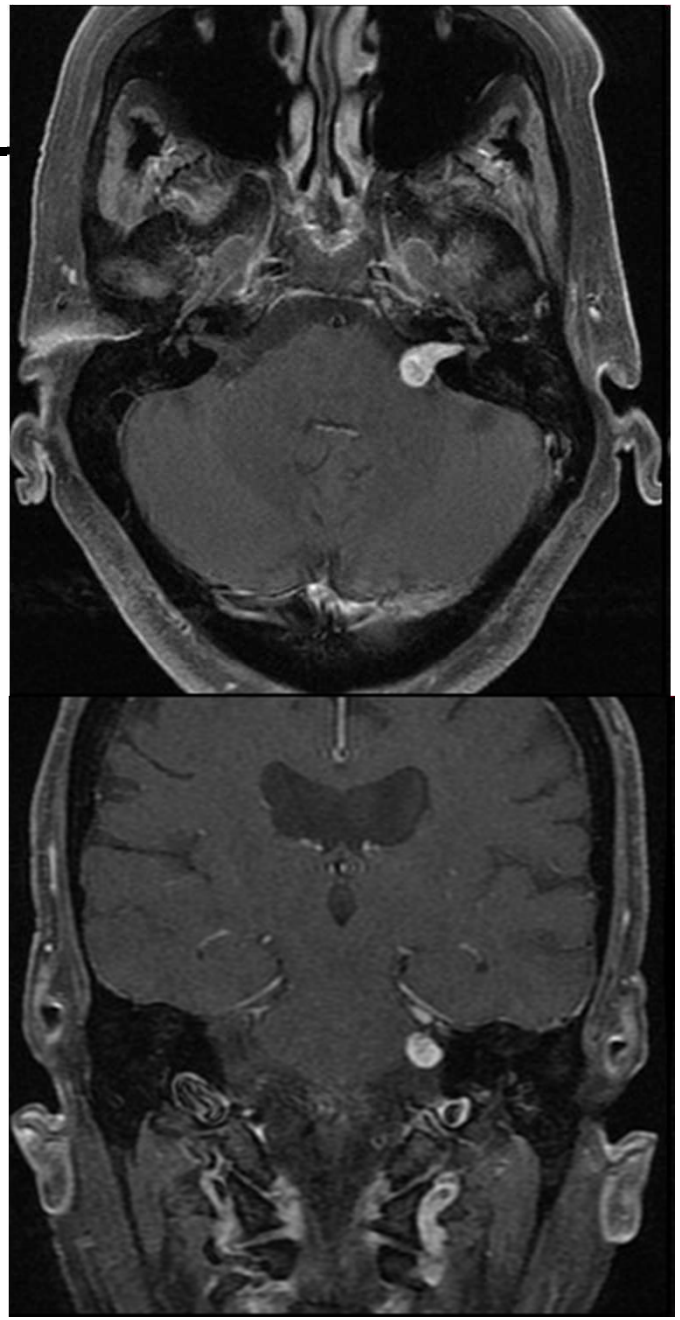

T1-w + Gd





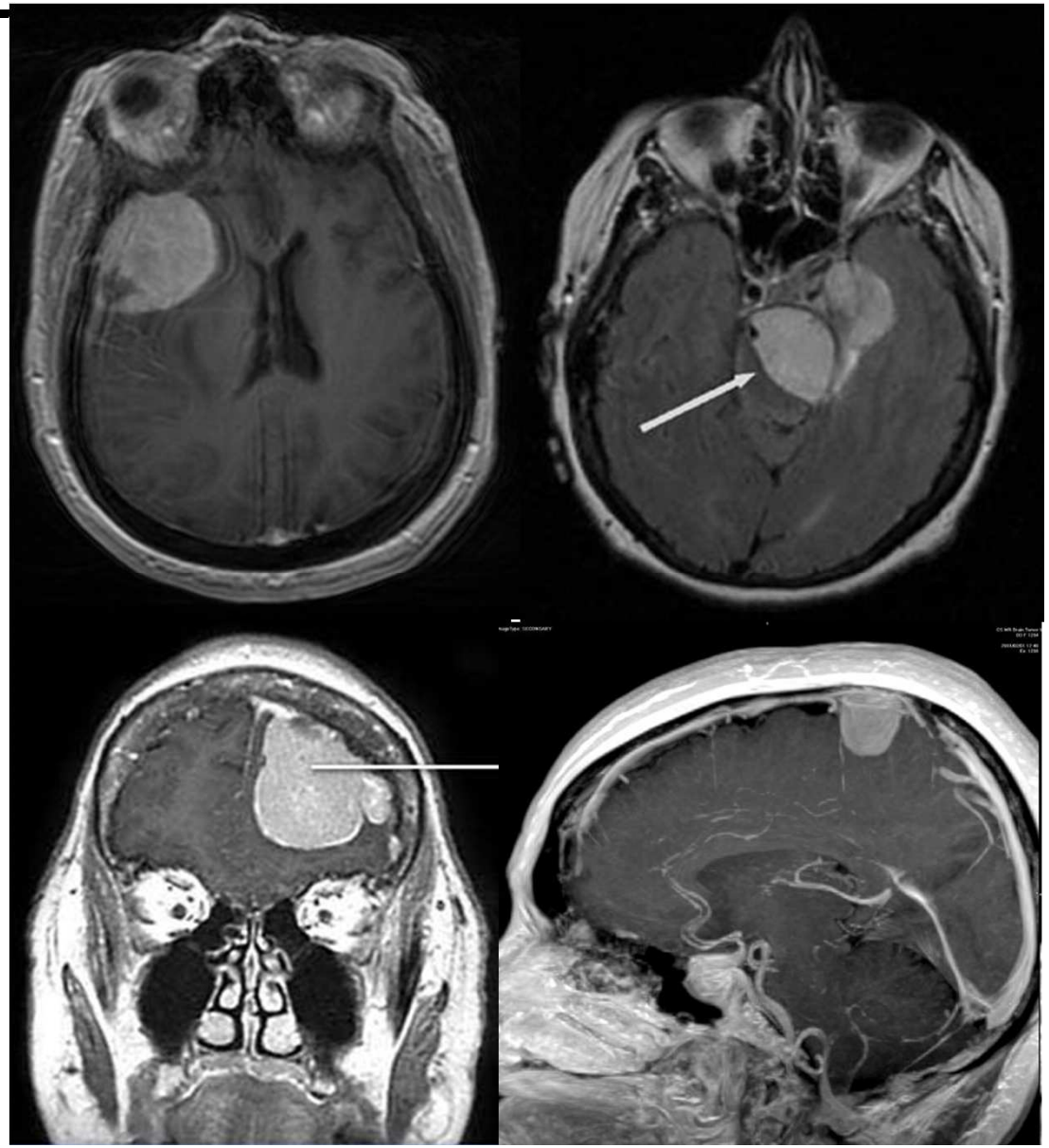
Acoustic Neuroma

- Benign tumor. Arises from VIII CN
- Slow growing (~1-4 mm/yr)
- Unilateral hearing loss, facial paresis, facial paresthesia, hydrocephalus
- Observation - till symptoms start bothering
- Radical surgery treatment of choice – damage to hearing and facial nerve
- Radiosurgery popular: radiation oncologists hardly get to treat this
- GTV = visible growth. No CTV. PTV according to immobilisation and technology (2-5mm)
- 21Gy/3fx, 40-48Gy, **50Gy/30fx**, 54Gy/30fx



Meningioma (WHO grade 1)

- Meningiomas, 90% are benign, can occur at any meningeal surface
- Complete surgical excision is curative: depends upon size, location (e.g. encompassing cranial arteries, venous sinuses) and general condition
- Incomplete surgery: recurrence is 30-70% @ 5 - 10 yrs, with further RT- 80-85% (No RCT, benefit unproven)



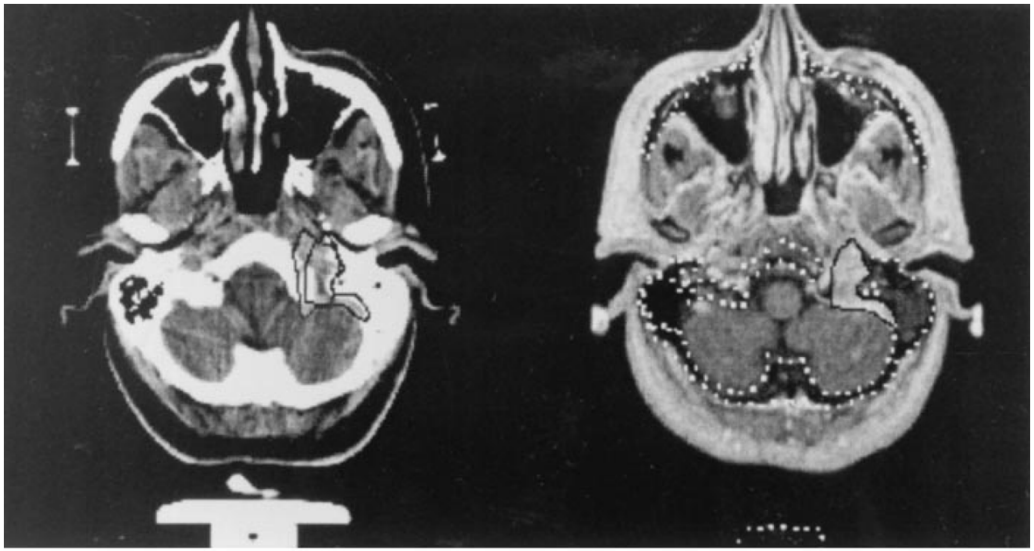
Meningioma (imaging needs and what to draw)

- Study pre and post operative imaging (plain and CECT, T1-w –plain and with Gd), in multiple planes to appreciate spread of tumor
- RTP scans at 2-3 mm, fused with T1-w post Gd scans
- GTV = enhancing mass AND abnormal bone presumed to contain active tumour (If this condition is met, then no need to draw a separate CTV)
- PTV = 3-5 or 10 mm margin according to immobilisation and technology
- Outline brainstem, eyes, optic nerves and optic chiasm
- Doses: 50 – 55 Gy at 1.8Gy/fx (55Gy/33fx)

Alheit et al, Radiother Oncol 50:145-50, 1999

Meningioma (imaging needs and what to draw)

- MR shows more soft tissue
- CT shows bone destruction better
- MR shows volumes larger but not inclusive of CT volumes: so contour on both and use the union (till we know better)



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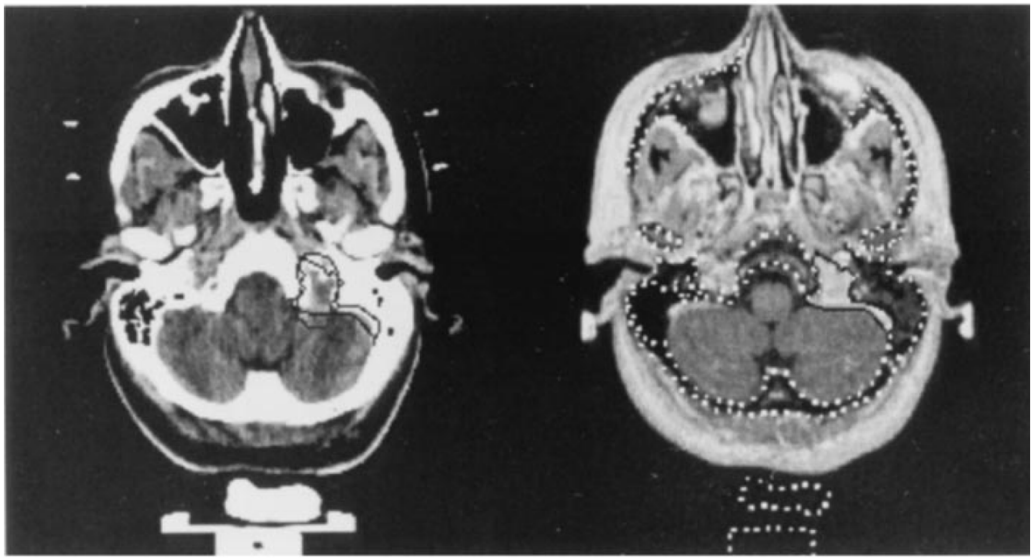
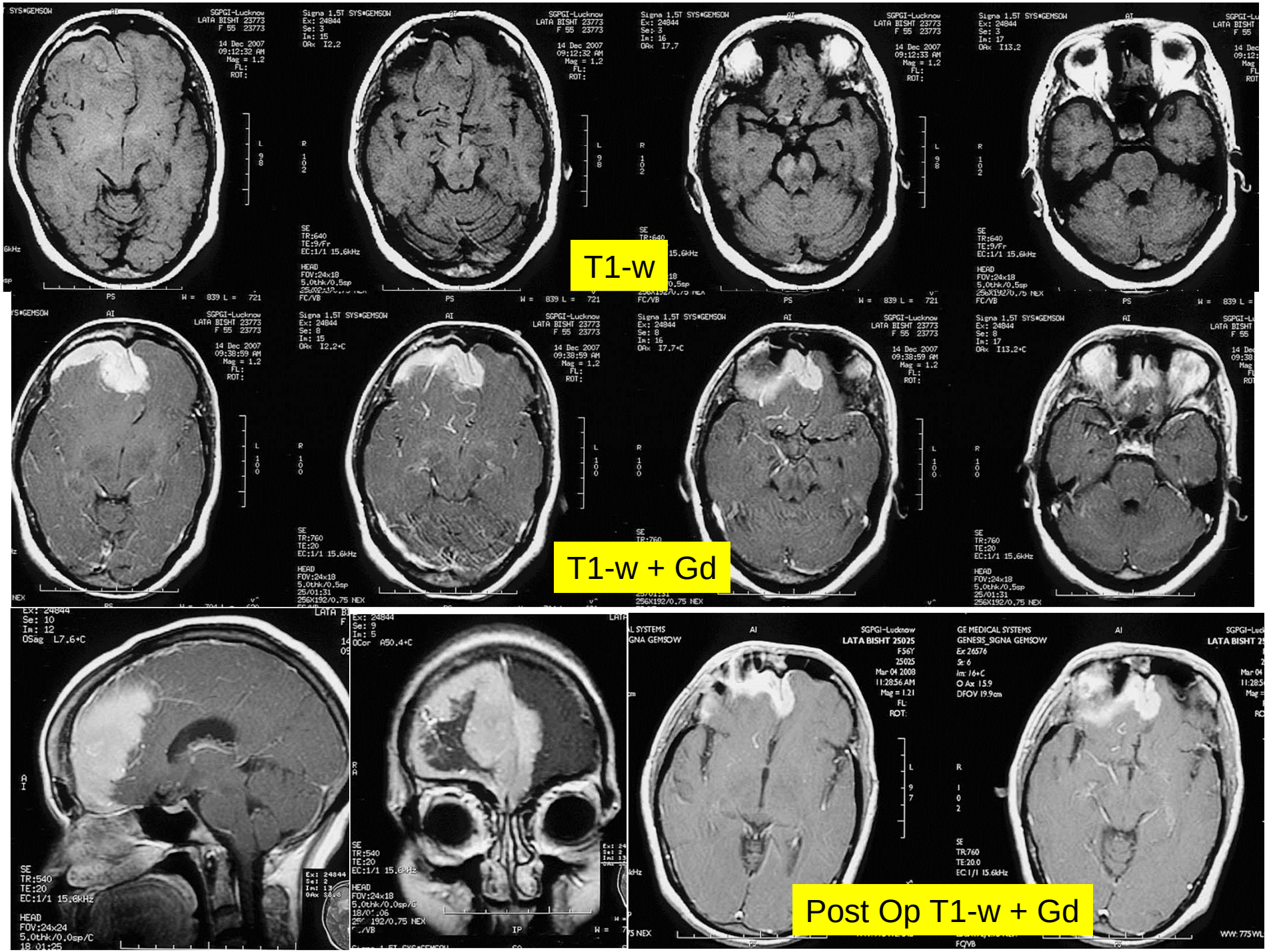


Khoo et al, IJROBP 46:1309-17, 2000


T1-w
T1-w + Gd
Post Op T1-w + Gd

GTV and CTV in gliomas

- This is the principal source of uncertainty in brain tumor RT (immobilization straightforward and organ motion minimal)
- MRI is better than CT
- Paucity of data which correlates imaging with microscopic extent of tumor
- Interpretation of imaging relies on pattern recognition, which is not fully evidence based
- Final proof of accuracy of tumor definition lies in the results of treatment policies employing specific target definition

Gliomas Grade III and IV (AA and GBM)

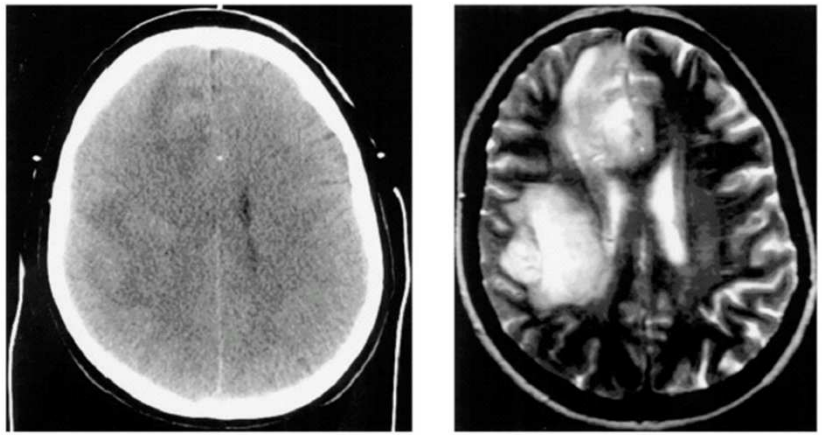
- Malignant gliomas enhance on CT and MR with mixed signal characteristics (high and low intensity regions)

- Contrast enhancement represents extravasation of contrast in areas of disturbed BBB, and this is assumed to correlate with high tumor cell density

- Region of enhancement is surrounded by low density areas (edema), which represents region of lower cell density, which may or may not contain tumor cells

Imaging and pathology

- Migration of cells along white matter tracts (corpus callosum)
- Also: though affected hemisphere; into other hemisphere; into brain stem
- Whole brain histological sections of 11 untreated GBMs and CT images compared
  - Tumor cells within low density in 6/11 and out side low density in 5/11
  - If presence of tumor cells is interpreted as CTV, extending low density by 1 cm would encompass 9/11. Add 3cm to cover 11/11
  - Contrast + 2 cm includes 8/11
- Between CT & MR, MR is better



Imaging and pathology..cont

n	GBM/AA	CT/MRI	Pathologic findings
35	Not specified	CT	CT within 2 months of death; 29/35 tumors within 2 cm of the tumor mass on CT
5	5/0	CT	In all cases neoplastic cells could be identified <3 cm from the periphery of the necrotic area on CT
15	15/0	CT	Eleven patients with antemortem CT; in 9/11 neoplastic cells outside contrast-enhancing ring on CT; margin of 3 cm around edema would have covered all tumor
40	8/7	CT/MRI	Fifteen of 16 biopsies from hypodense area on CT and T2 prolongation on MRI contained tumor cells; 14/14 biopsies from isodense area on CT and T2 prolongation on MRI showed tumor cells
18	6/12	CT/MRI	Nine of ten biopsies from normal areas on CT and hyperintense area on T2-MRI contained tumor cells; in 4/18 patients tumor cells were found beyond hyperintense area on T2-MRI
5	3/2	MRI	White matter edema on T2-MRI correlated 100% with tumor extension; MRI underestimated gray matter and subarachnoid space infiltration in three of five patients

Volume in relation to clinical and pathological information

- Recurrences are seen in 80% within 2cm of enhancing region
- Based on pathological information of tumor extent CTV would need to be 3 cm beyond hypo-density or 5 cm beyond region of enhancement.
- If using CRT, could define 3 volumes !
- Practical model: CTV is 2-3 cm beyond enhancement. Make allowance for known migration patterns. Restrict for anatomical barriers.

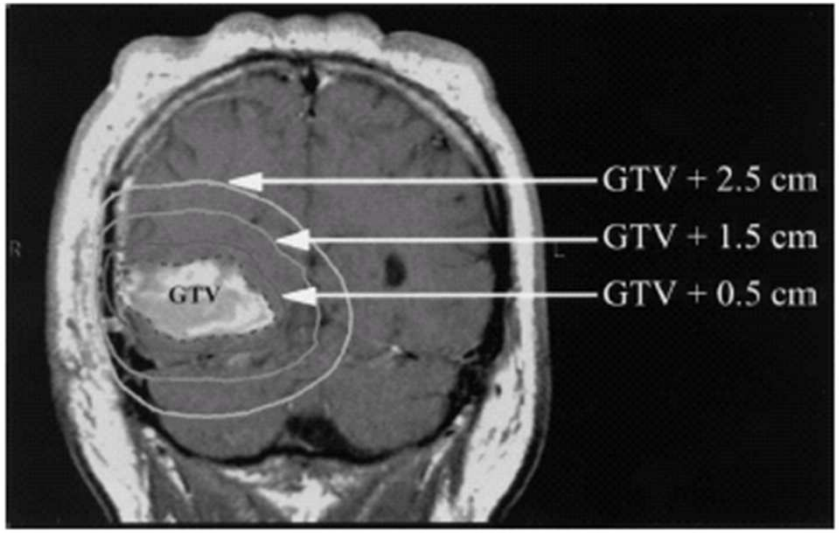


Fig. 1. Representative PTV definitions: PTV1 = GTV + 0.5 cm; PTV2 = GTV + 1.5 cm; PTV3 = GTV + 2.5 cm (see text).

Ten Hakenet al. IJROBP 1998:42:137

Volume in relation to outcome (survival)

- Whole brain (6020cGy/35#/7wks) vs WB 4300cGy/25# Plus ?enhancing tumor +2cm (1720/10#). No survival disadvantage
- Brachy boost, identical survival
- Radiosurgery boost, identical survival
- These studies confirm that it is appropriate to define CTV relatively close to the region of enhancement

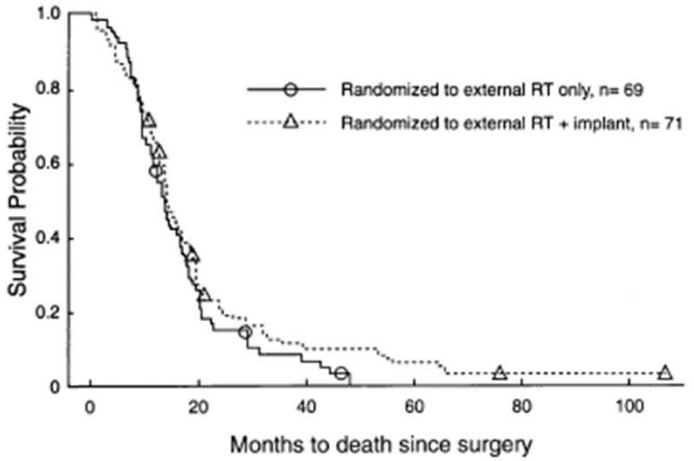


Fig. 1. Survival curves for both arms of the study. Log rank p-value = 0.24.

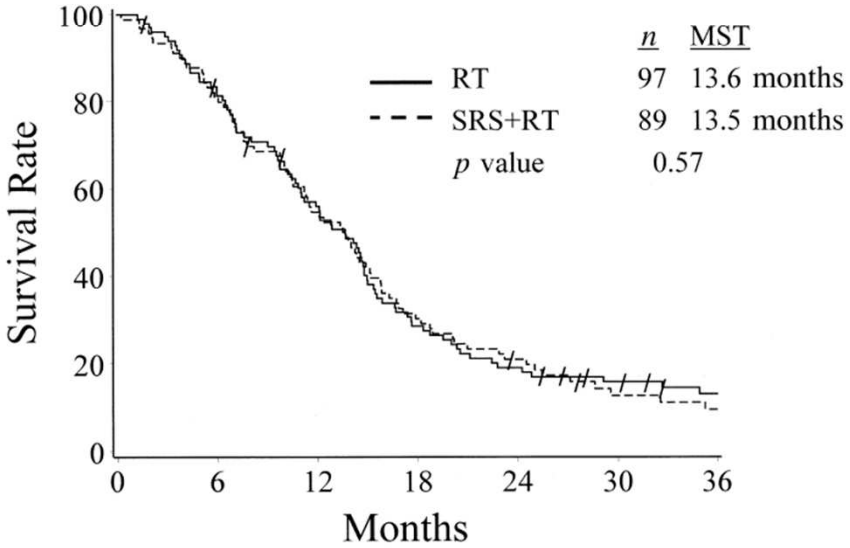


Fig. 1. Survival by treatment arm. RT = radiation therapy; SRS = stereotactic radiosurgery; MST = median survival time.

Volume in relation to outcome (recurrence)

Table 6. Recurrence patterns at death

	Nonimplant arm [number (%)]	Implant arm [number (%)]	Total (%)
Original site (OS)*	64 (93)	58 (82)	122 (87)
OS + multifocal	0	5	
OS + meningeal	1	1	
OS + hematogenous	0	2	
Other causes of death†	1	7	8
Alive at time of analysis	4	6	10
Total	69	71	140

* CT enhancement at recurrence that incorporates at least part of original tumor volume.

Lapperriere etal. IJROBP 1998;41:1005

Table 3. Patterns of failure

	Radiation therapy (n = 96)	Stereotactic radiosurgery + radiation therapy (n = 89)
Local only	51 (67%)	42 (58%)
Adjacent only	4 (5%)	2 (3%)
Local + adjacent	16 (21%)	18 (25%)
Nonadjacent only	0	1 (1%)
Local + nonadjacent	2 (3%)	1 (1%)
Local + adjacent + nonadjacent	3 (4%)	5 (7%)
Unknown	0	4 (5%)
No failure	20	16

Souhami etal. IJROBP 2004;60:853

Volume in relation to outcome (recurrence)

n	GBM/AA	Pre-/post-RT CT	Radiation treatment technique	Recurrence pattern
1035	405/630	Post	WBI	95% of GBM and 91.4% of AA recurred at the site of the primary tumor
42	Not specified	Post	WBI	80% recurrence within 2 cm of enhancing mass; 10% partly within 2 cm
34	25/9	Pre	WBI; in 25 patients + cone-down boost to 'tumor bed'	78% within 2cm of enhancing edge on CT; 22% > 2.0 cm
70	48/22	Pre	WBI + boost	72% within the boost field to enhancing mass plus 2 cm; 23% partly outside boost field
60	39/21	Pre	Seven patients WBI; 53 patients PBI	93.7% (45 patients) had recurrence in radiation fields, i.e. contrast-enhancing mass plus 3 cm, in 48 patients, with follow-up CT
66	Not specified	Pre	2 cm beyond enhancing mass	86% recurred in the PTV, i.e. contrast-enhancing mass plus 2 cm, in 58 patients, with recurrence documented by CT
36	23/13	Pre	Two patients WBI; 34 patients PBI	Majority of local recurrence at the primary site, i.e. zone of prolonged signal on T2-MRI plus 2.5–3.0 cm

What should be the GTV, CTV and PTV for HGG?

- RTOG: Phase I: T2 +2.0cm, Phase II: T1w contrast enhanced +2.5 cm
- MRC: T1w contrast + 3cm (single plan)
- Post operative imaging preferable as
  - Debulking reduces volume of GTV
  - Brain and residual tumor change position
  - Steroids reduce mass by reducing edema

GTV: Contrast enhancing edge

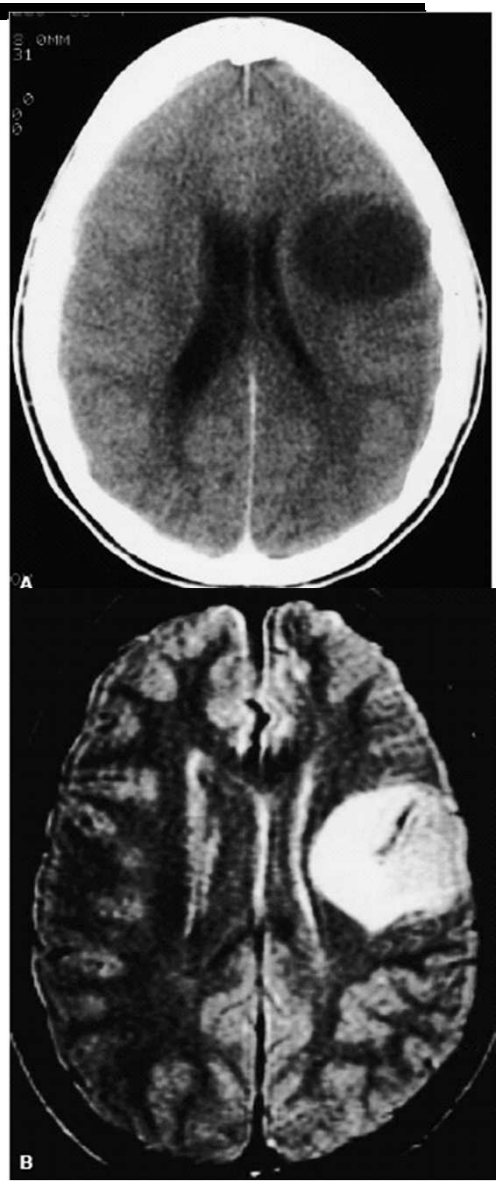
CTV: Phase I = GTV + 2.5 cm

Phase II = GTV + 1.5 cm

PTV: CTV + 0.5 cm

Grade II (fibrillary astrocytoma and oligodendroglioma)

- Do not enhance
- CT scan shows low density abnormalities with diffuse edges
- FLAIR shows high signal intensity, but this may merge with normal brain.
- It is assumed that the FLAIR sequence high intensity area represents regions of high tumor density



What is the GTV, CTV and PTV for adult LGG?

- Low vs high dose (50.4 vs 64Gy)
  T2 + 2cm (50.4Gy) and T2 + 1cm (boost to 64Gy)

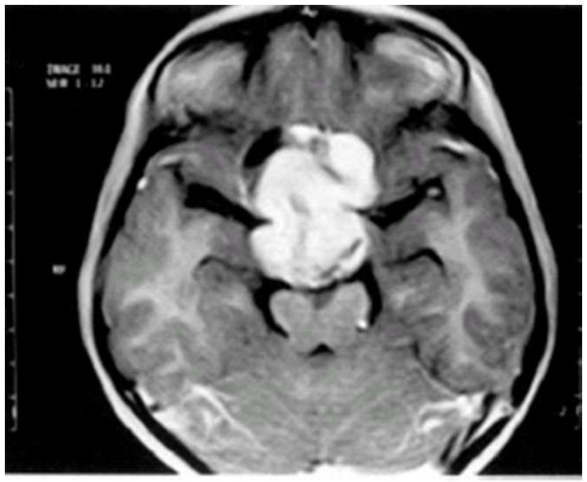
- EORTC early vs delayed RT
  Hypodensity + 1cm (45Gy), reduce margin by 1cm to 54 Gy

- EORTC 45 vs 59.4Gy
  Hypodensity + 1cm (45Gy), reduce margin by 1cm to 54 Gy

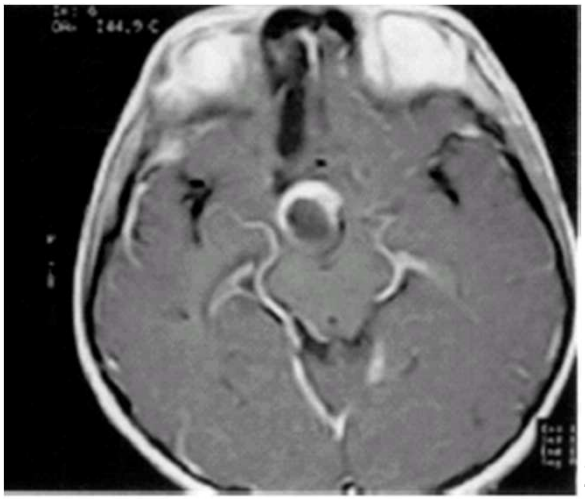
GTV:	High signal on T2 or FLAIR (low density on CT)
CTV:	GTV + 1.0 -1.5 cm
PTV:	CTV + 0.5 cm

GTV and CTV for paediatric low grades

- GTV = tumor / presumed tumor
- CTV: add 5 mm in 3D
- PTV: add 5 mm for mask system and 2mm for SCRT



- Dose 54Gy/30#
- Followup median:25mo (12-47)
- 3 yr DFS 96%



Jalali et al. R&O 2005

Conclusion

- Imaging should include both CT and MR and studied carefully in all planes
- RTP scans are 2-3 mm with contrast (except pituitary) and fuse with contrast enhanced MRI when available
- For pituitary, acoustic, meningioma (WHO Grade 1) and craniopharyngeoma: GTV is what you see post operatively and include presumed tumor, such as shaved off bones, or cyst cavities
- The need to expand to CTV is then not necessary
- T1-w + contrast + a margin 2.5-3.0 to PTV is adequate for HGG
- Flair image + 1.0 -1.5 cm margin to PTV adequate for LGG
- PTV expansion is based on immobilisation and radiation equipment in the main