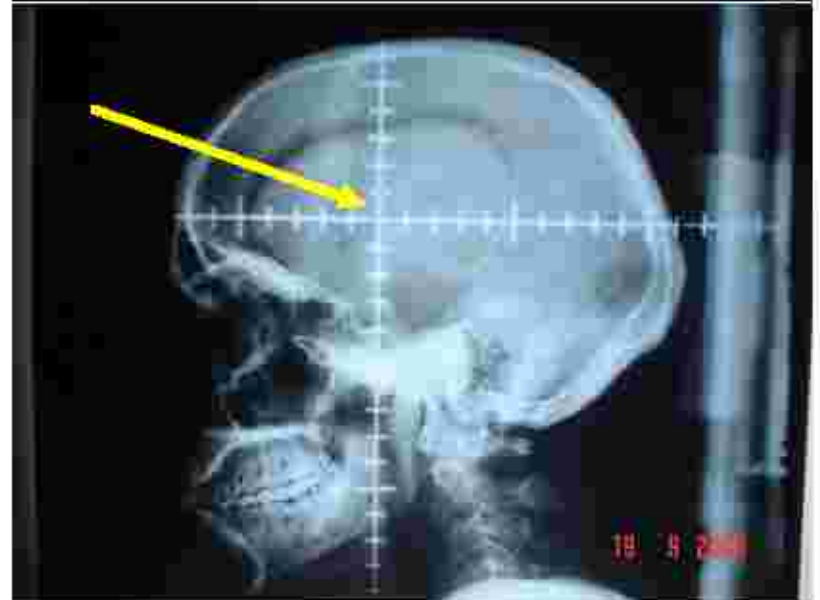
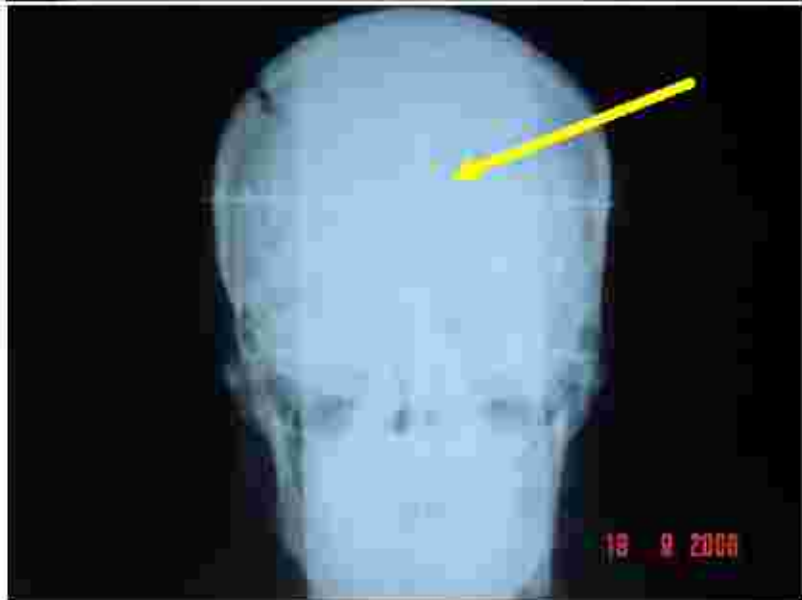
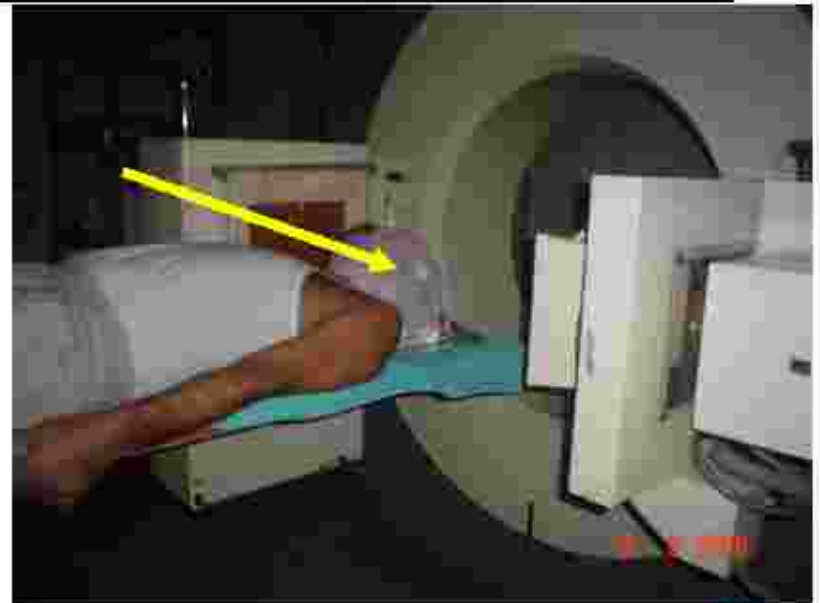


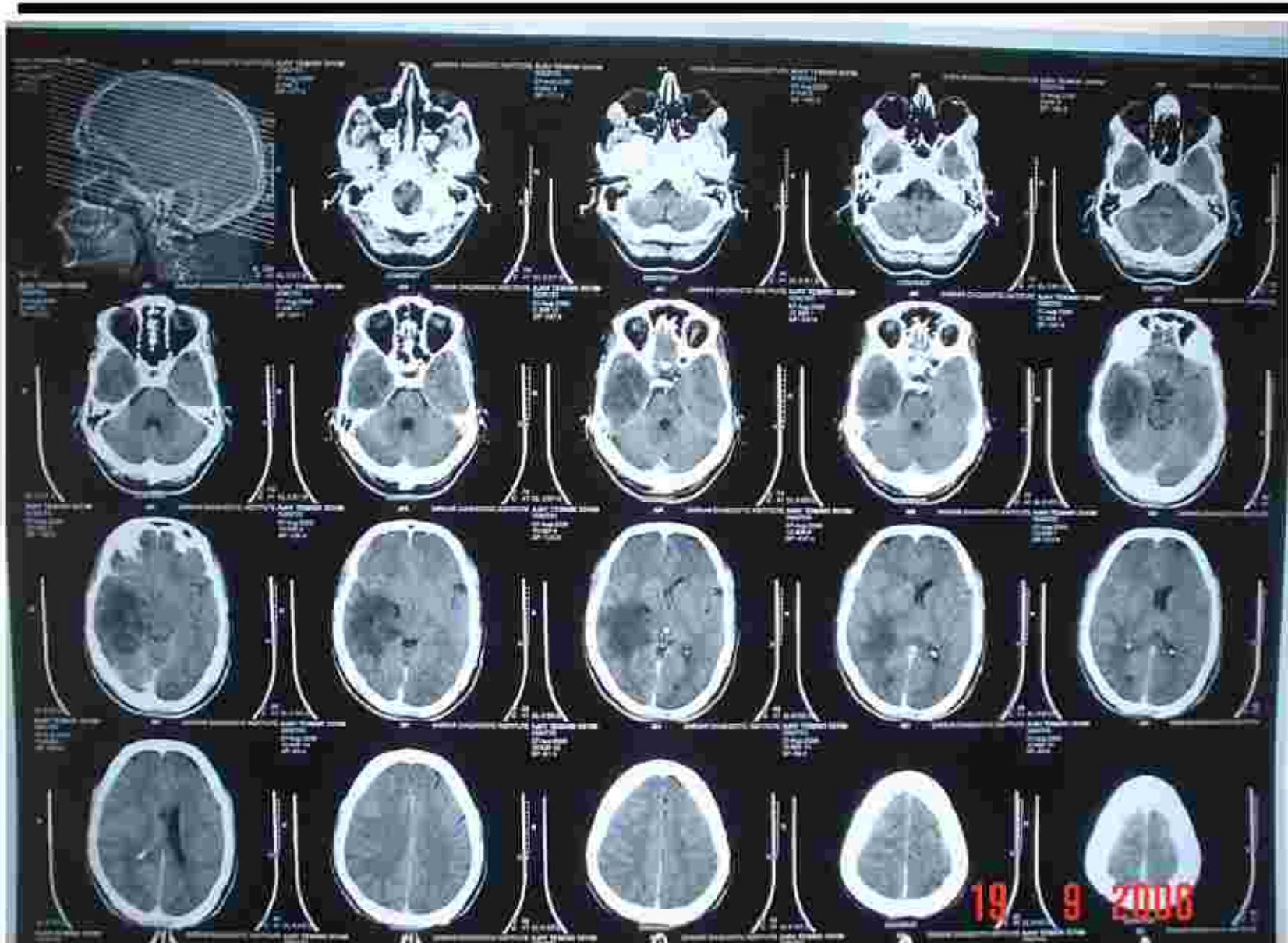
Conventional reconstruction and planning of gliomas

- Use a CT scan to construct a tumor volume on a simulation film
- Superimposition of sagittal MR on lateral skull simulation films
- Potential pitfalls in reconstruction
- What should be the GTV, CTV and PTV for HGG and LGG?

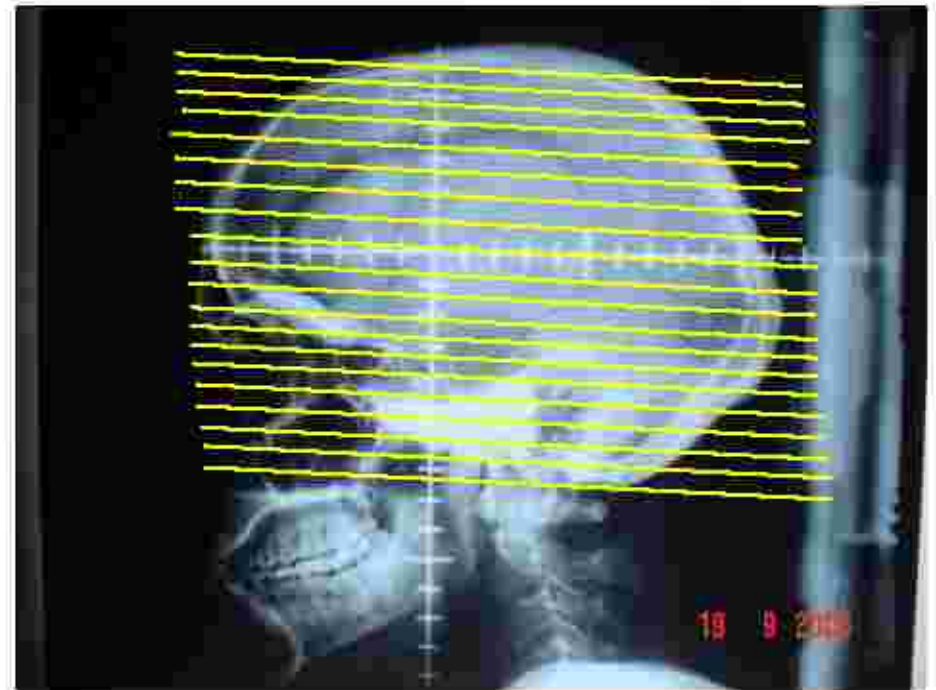
Conventional orthogonal plain film planning



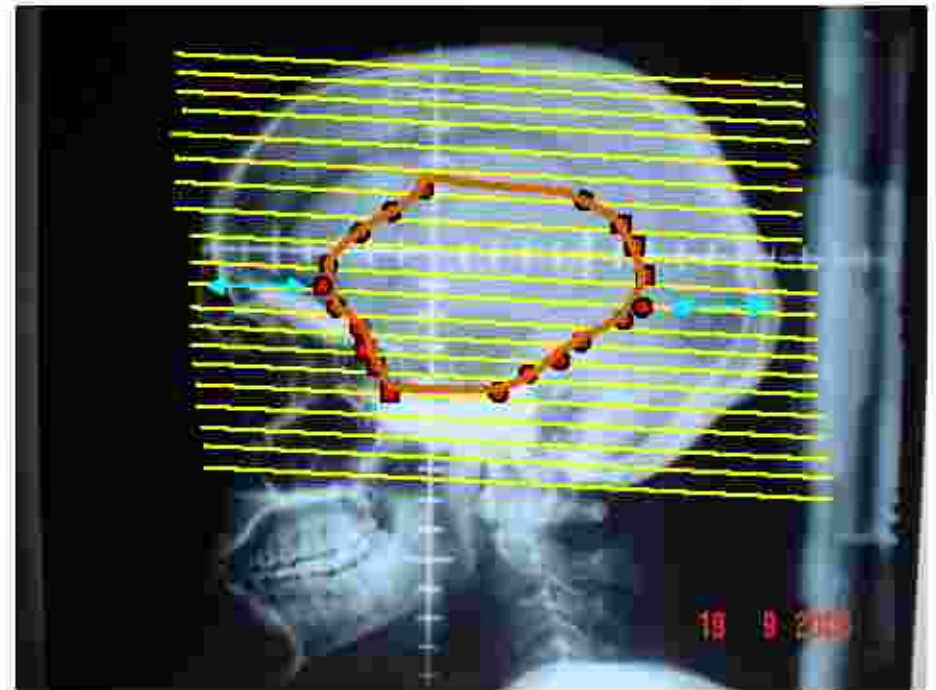
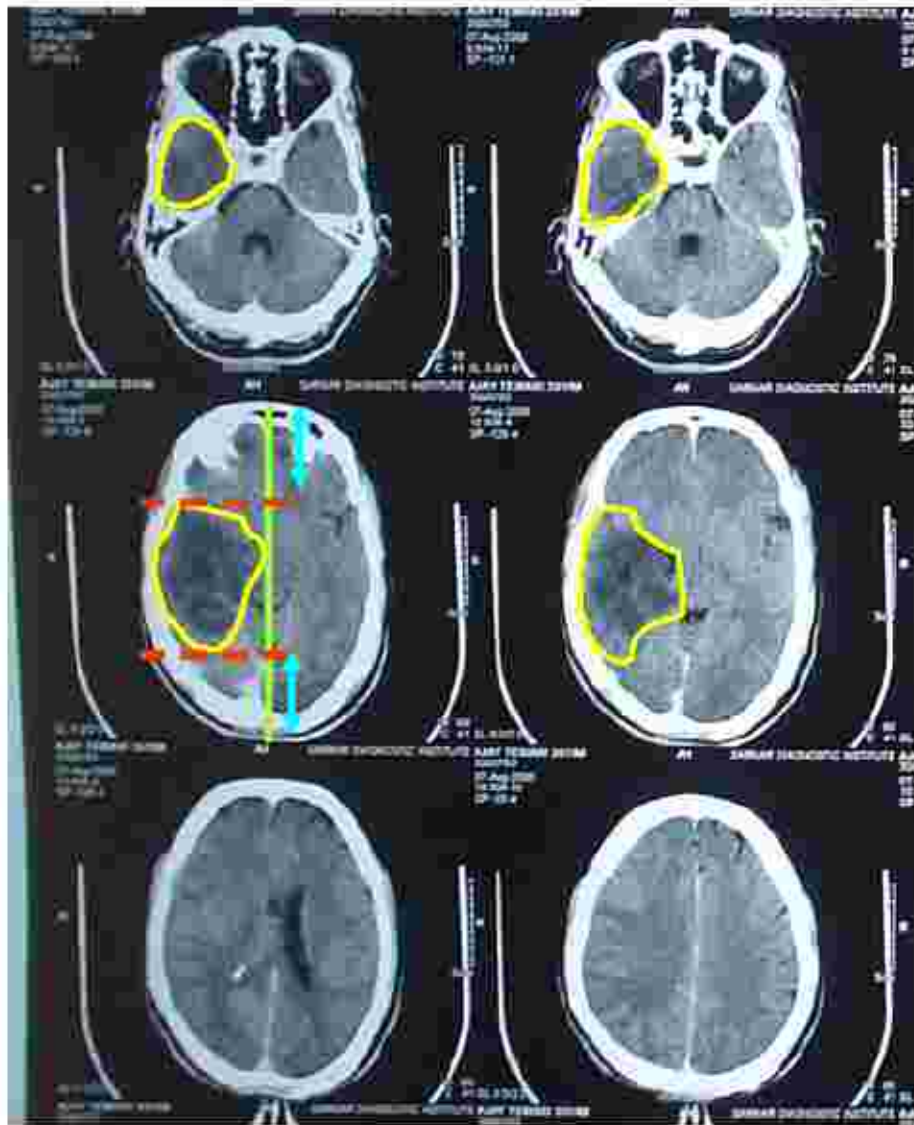
View CT image



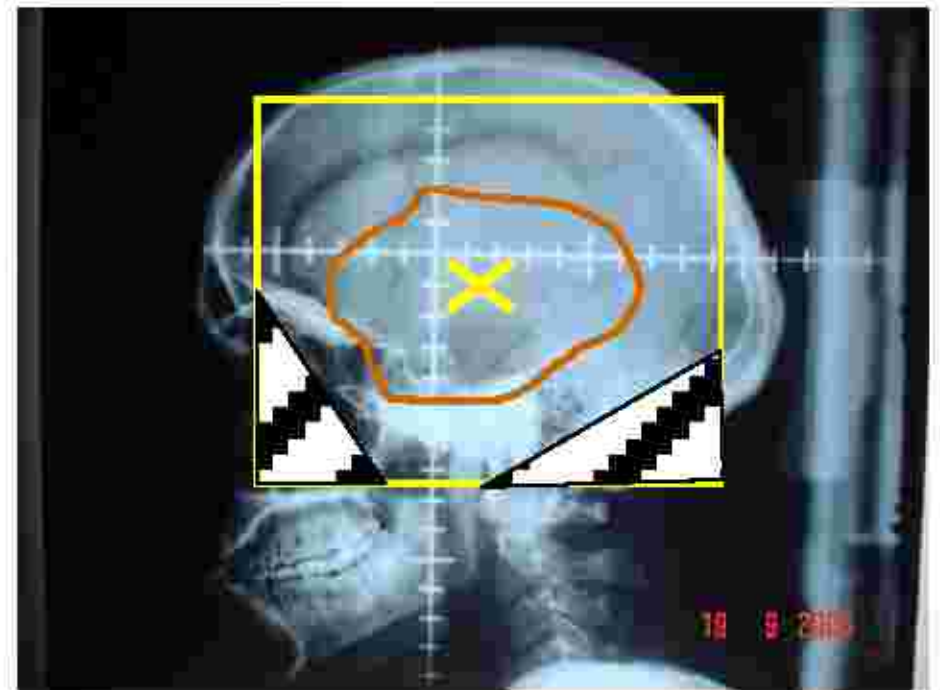
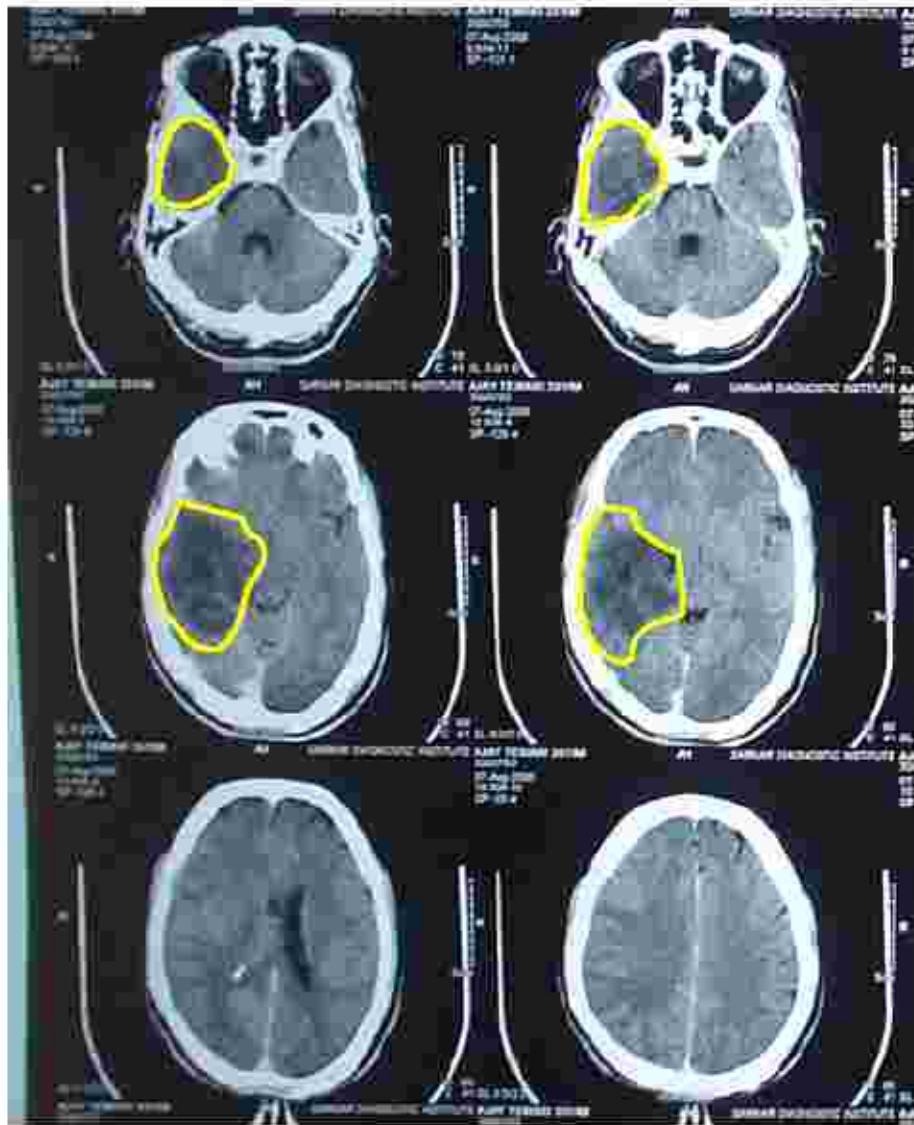
View scout film, transfer slices onto simulator film



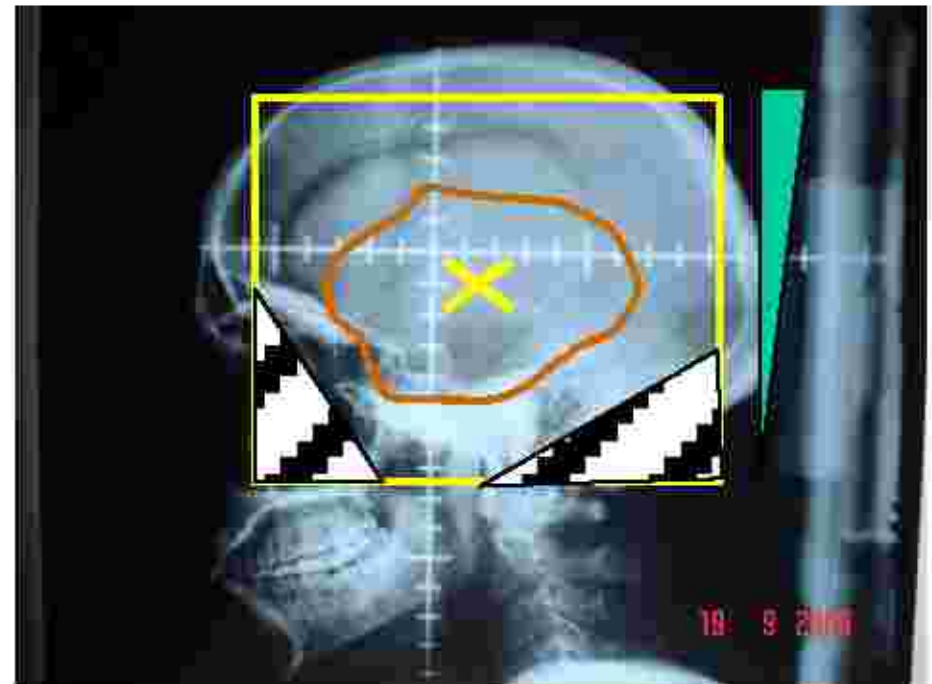
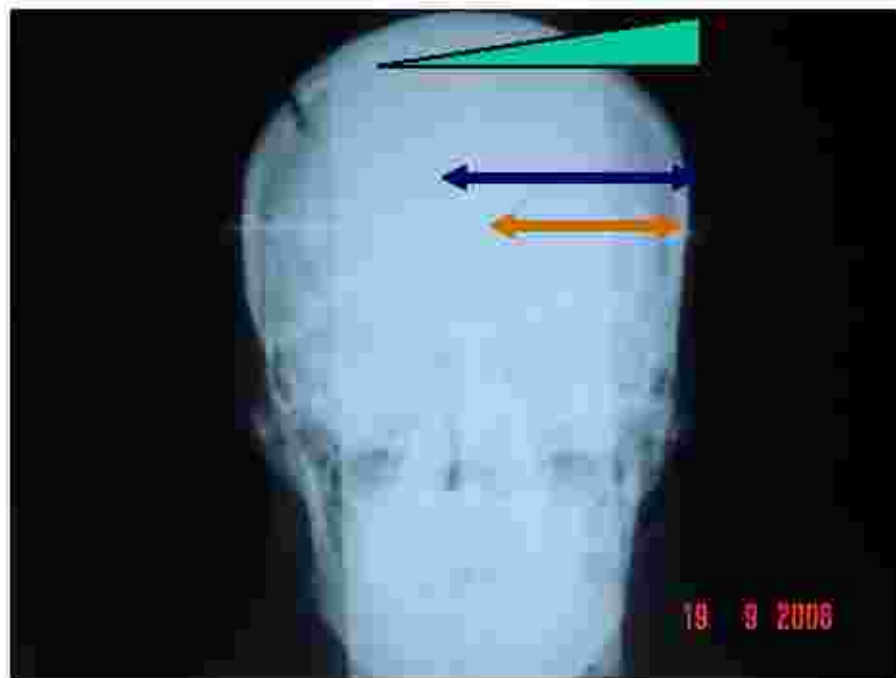
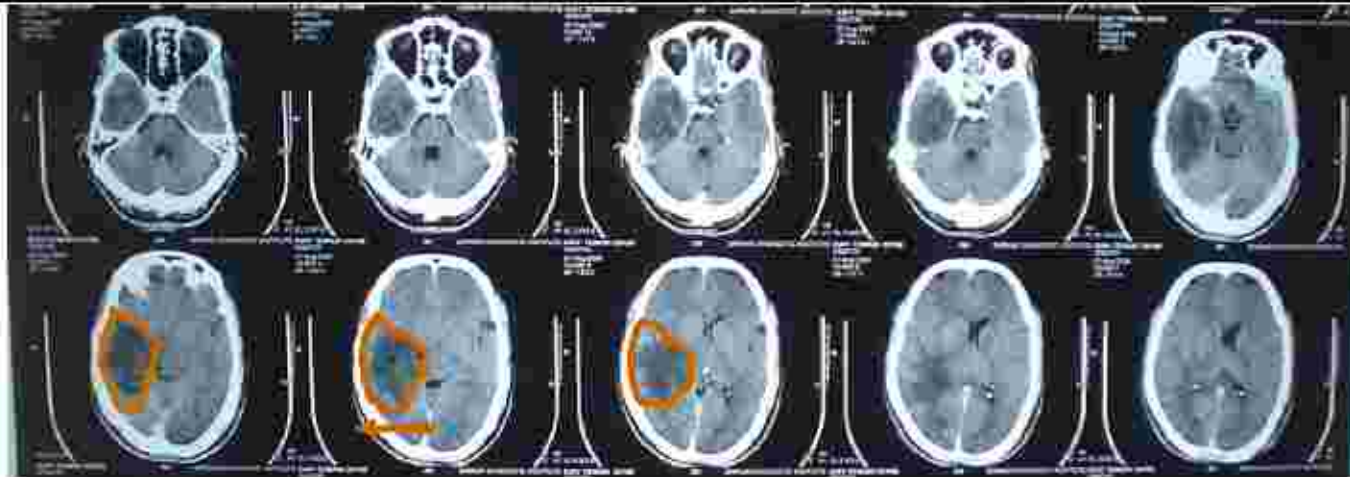
Contour target outline



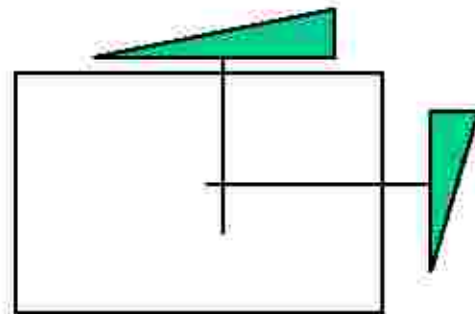
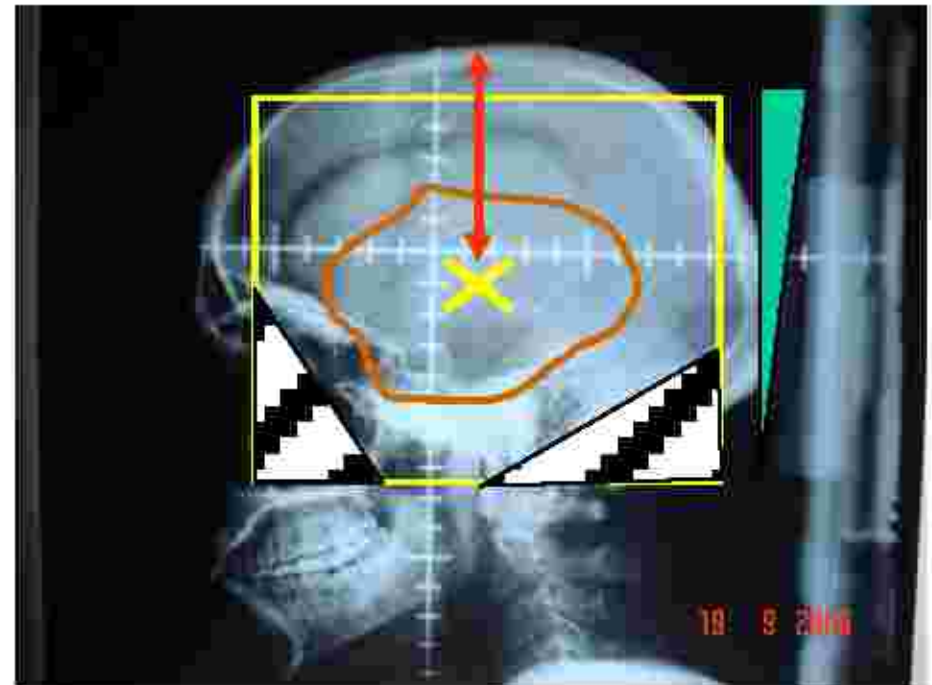
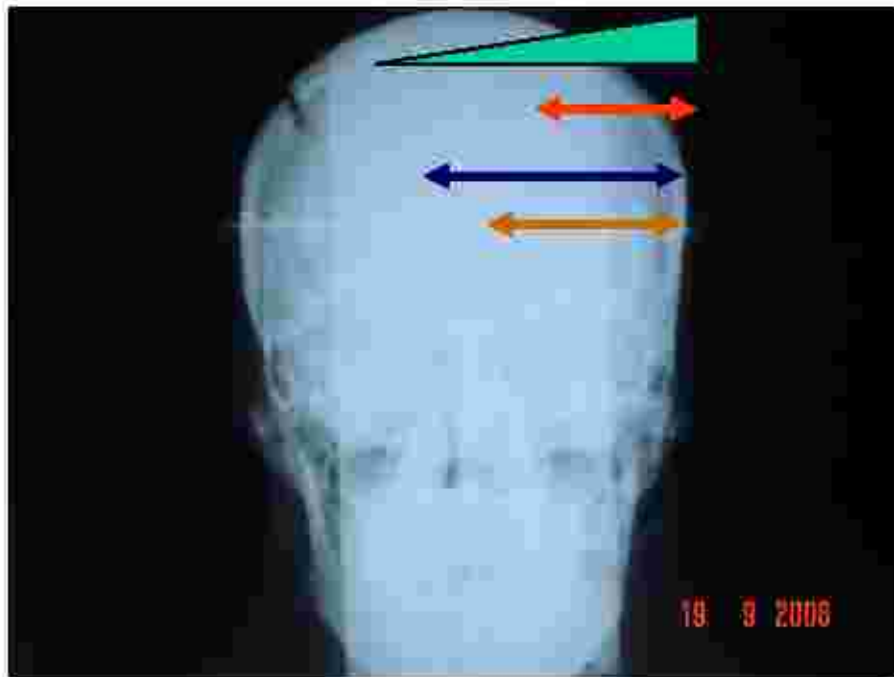
Place a field



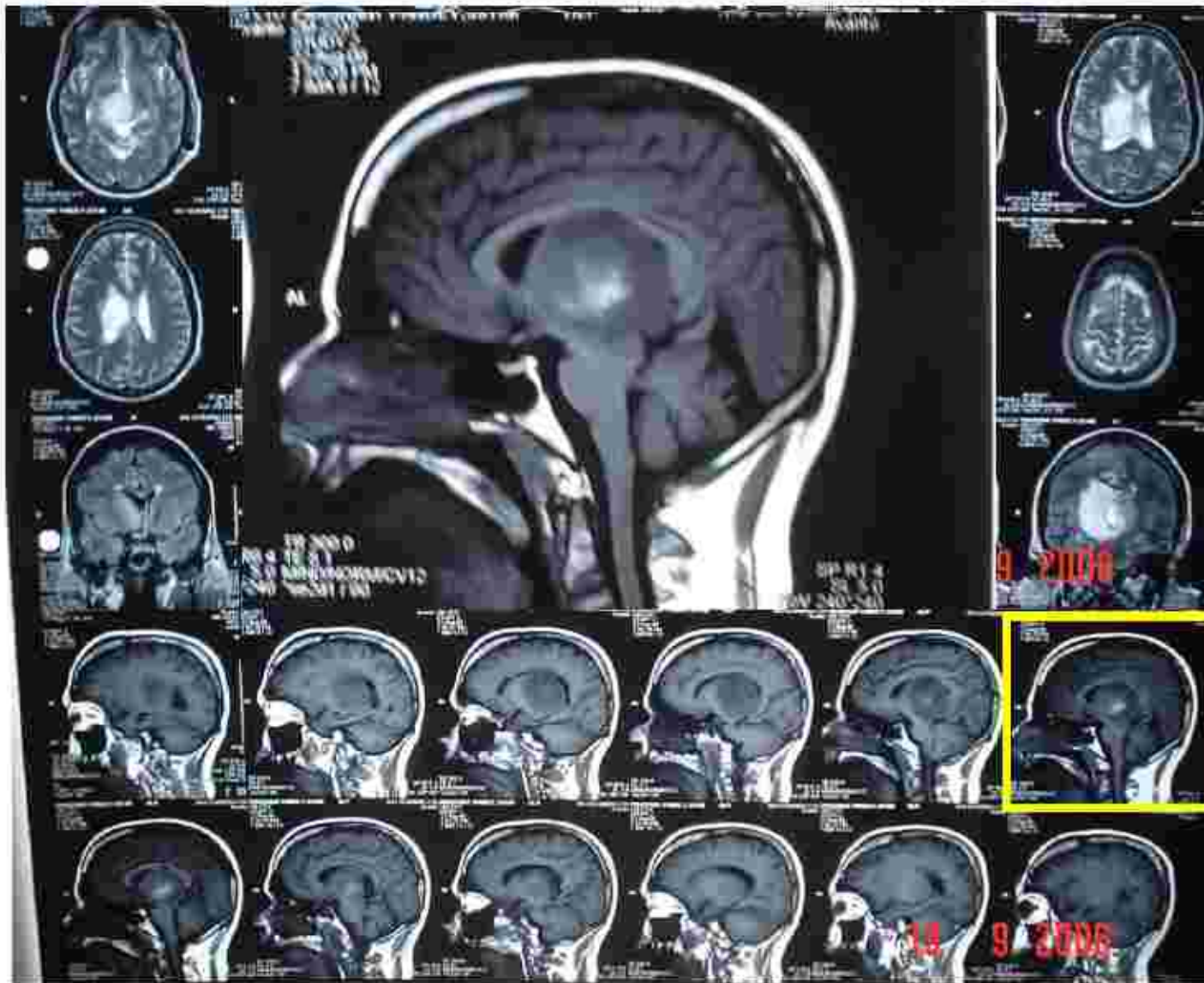
But instead of a parallel pair could we do better?



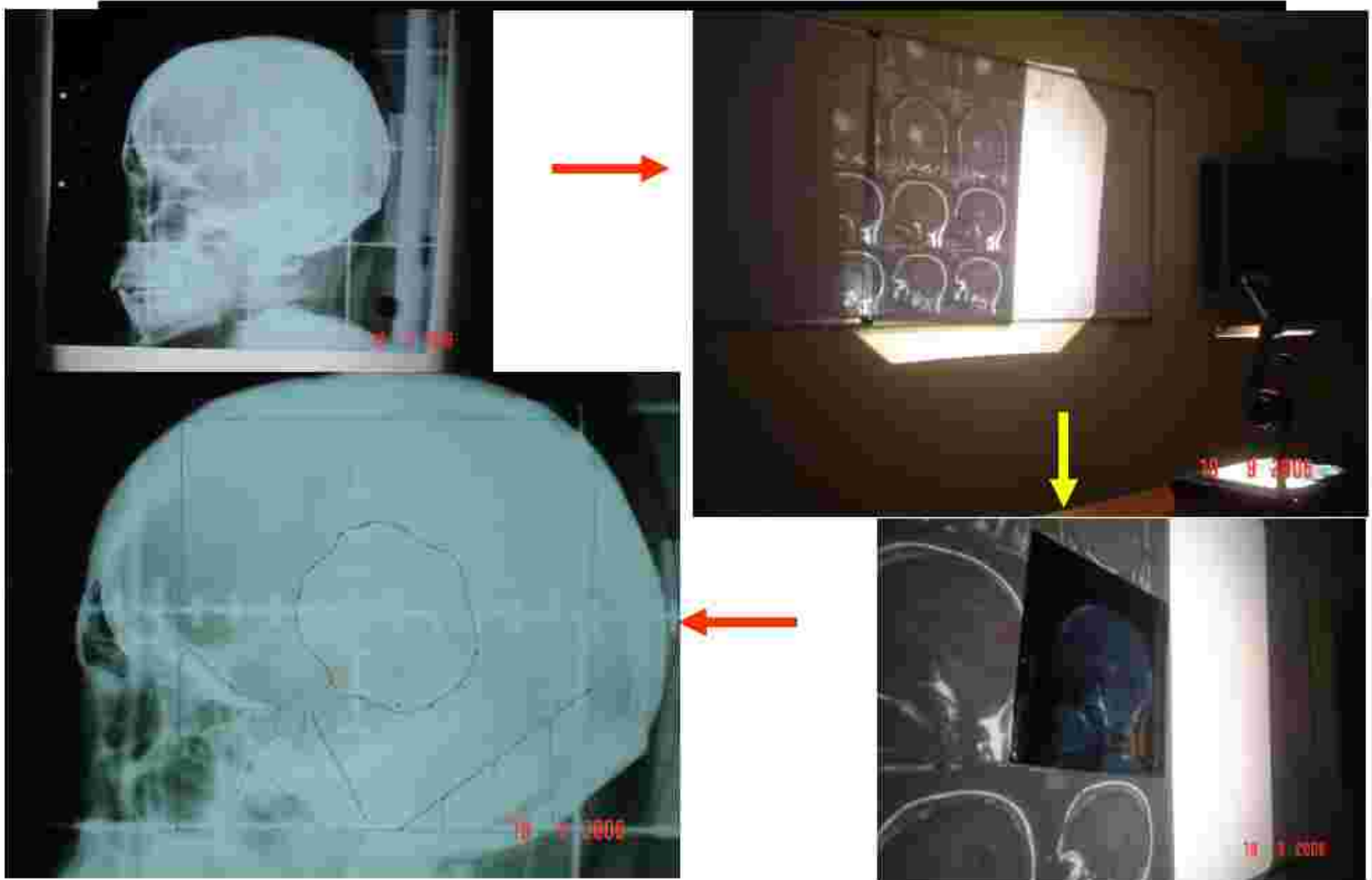
And where do you prescribe?



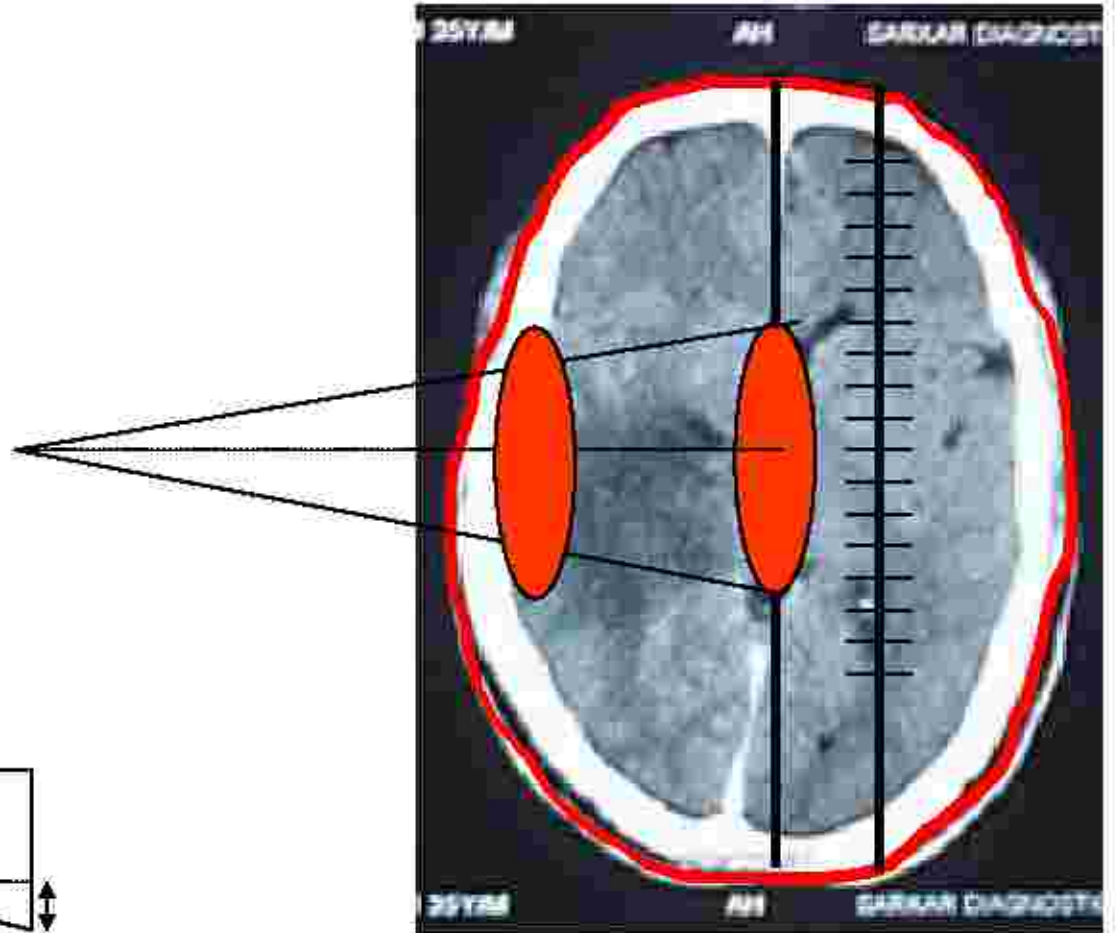
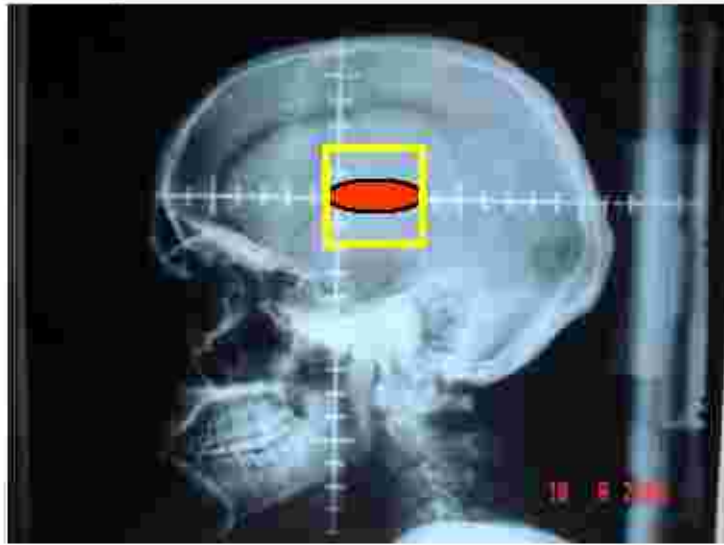
Sagittal MR on lateral simulation films



Transpose sagittal image onto simulator film



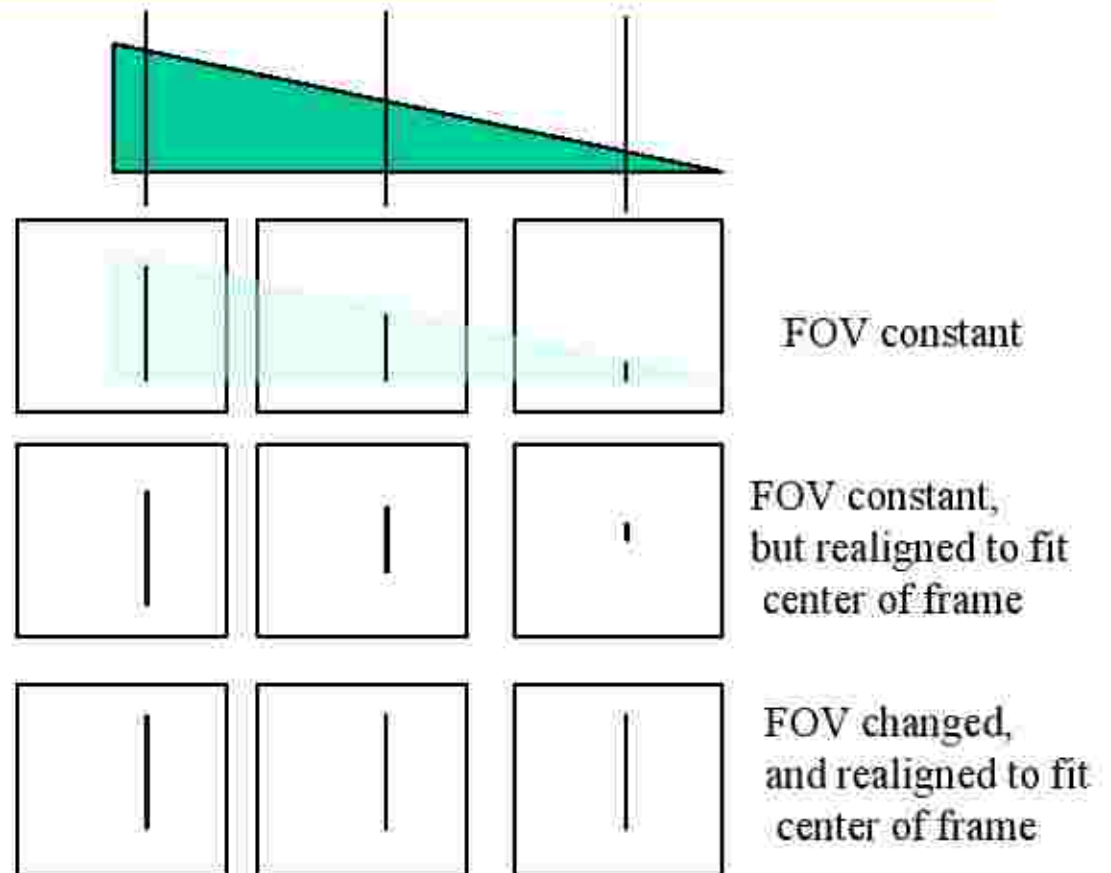
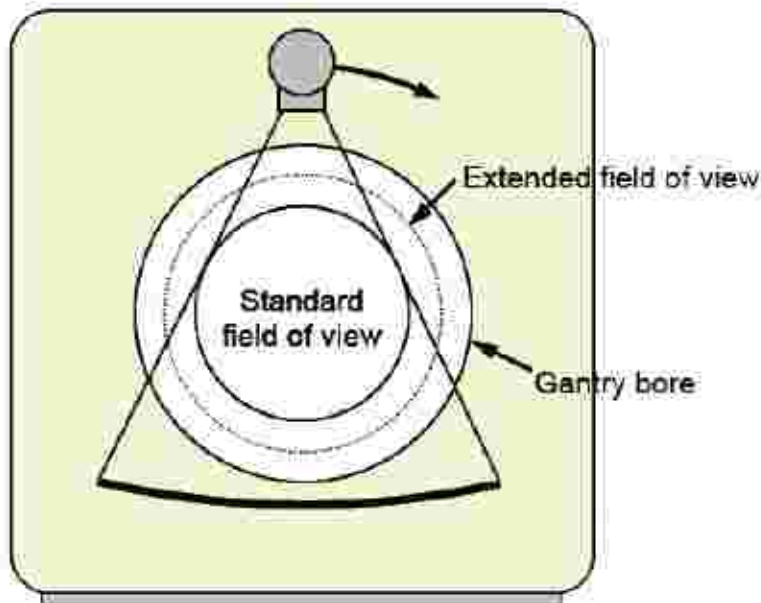
Pitfalls in reconstruction

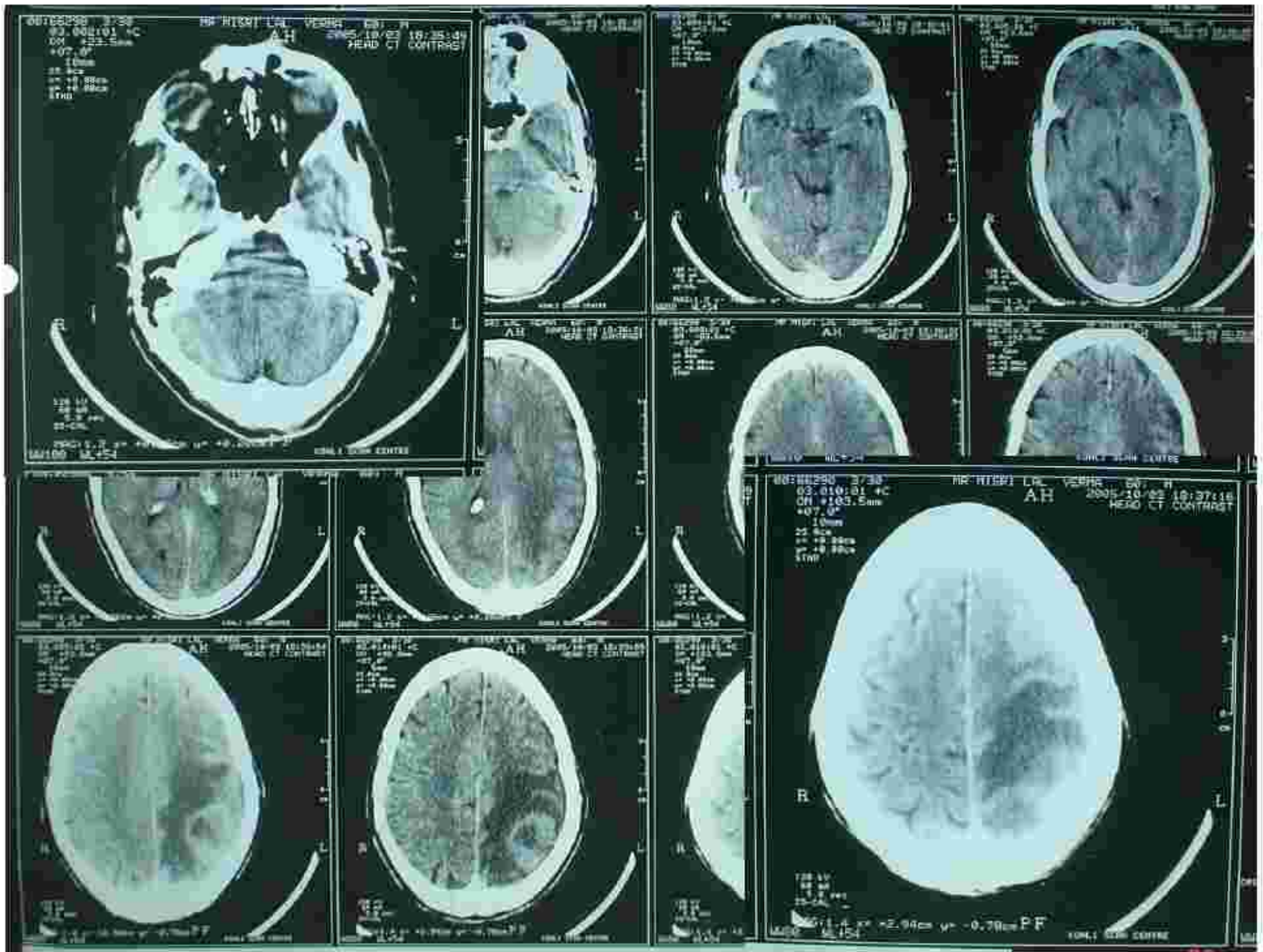


0.6mm (5cm), 1.5mm (7.5cm), 2.6mm (10cm), 2.5mm (12.5cm)

Another problem: Changing FOVs

Field of view (FOV) is defined as the maximum diameter of the reconstructed image. Its value can be selected by the operator and generally lies in the range between 12 and 50 cm.





Other problems

1. Errors in measuring the size on CT scan
2. Errors in redrawing on simulation film
 - Combined errors of 1 & 2, estimated by measuring mean distance between isocentre established by manual transfer as opposed to CT simulator is of the order of 6mm +/- 4mm
3. Conventional vs. CT planned:
 - PTV reduced by 23%
 - Shift in entry points for lateral beams Sup-inf: 1.3 cm; ant-post: 0.8cm
4. Errors in repositioning the treatment fields each day (unrelated issue)

GTV and CTV in brain tumors

- 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 outside 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

<i>n</i>	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.

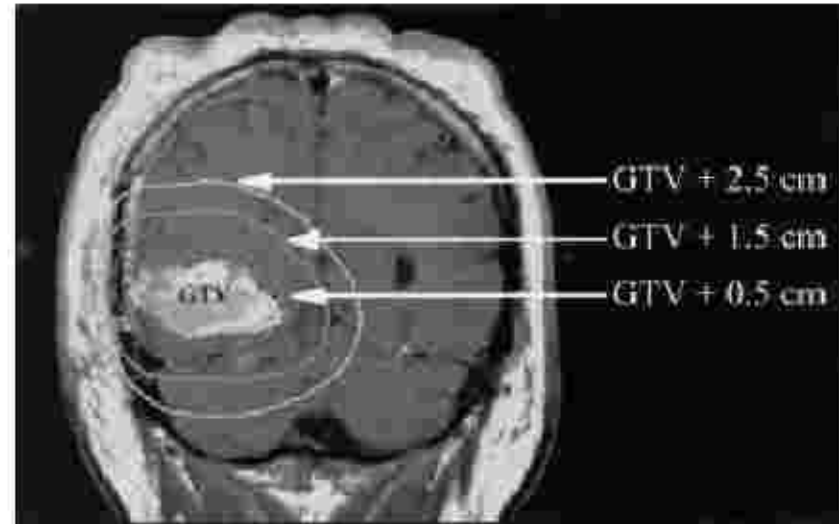


Fig. 1. Representative PTV definitions: PTV1 = GTV + 0.5 cm; PTV2 = GTV + 1.5 cm; PTV3 = GTV + 2.5 cm (see text).

Ten Haken et 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

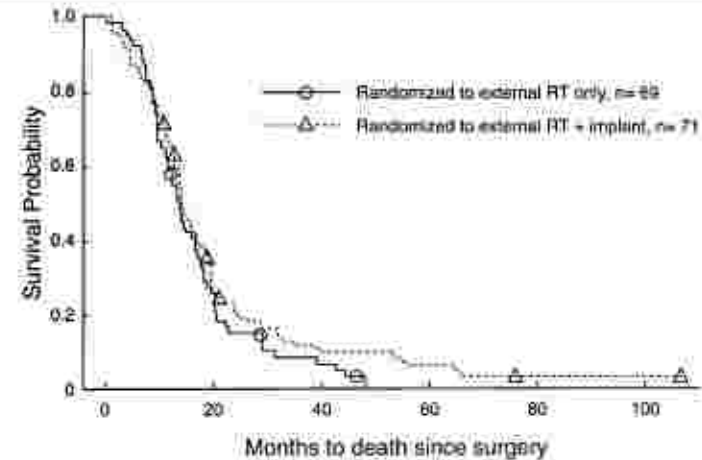


Fig. 1. Survival curves for both arms of the study. Log rank p -value = 0.24.

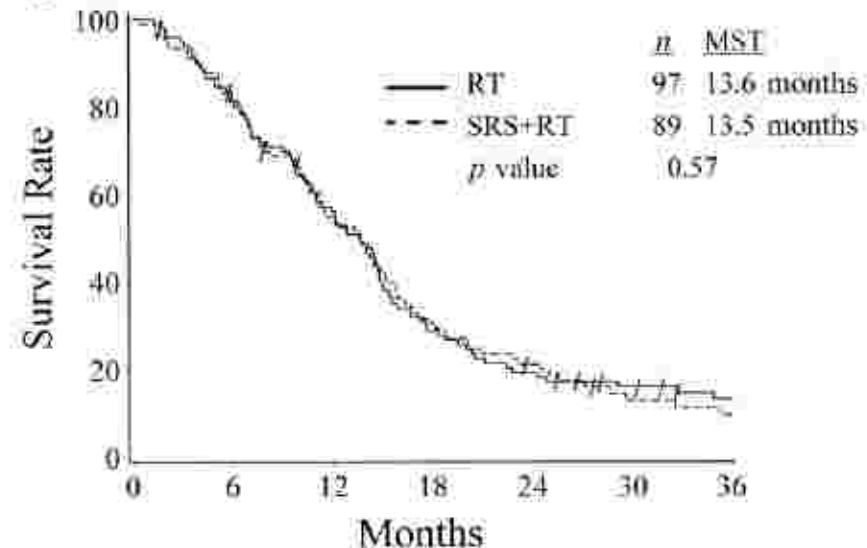


Fig. 1. Survival by treatment arm: RT = external beam; SRS = stereotactic radiosurgery; MST = median survival.

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.

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

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

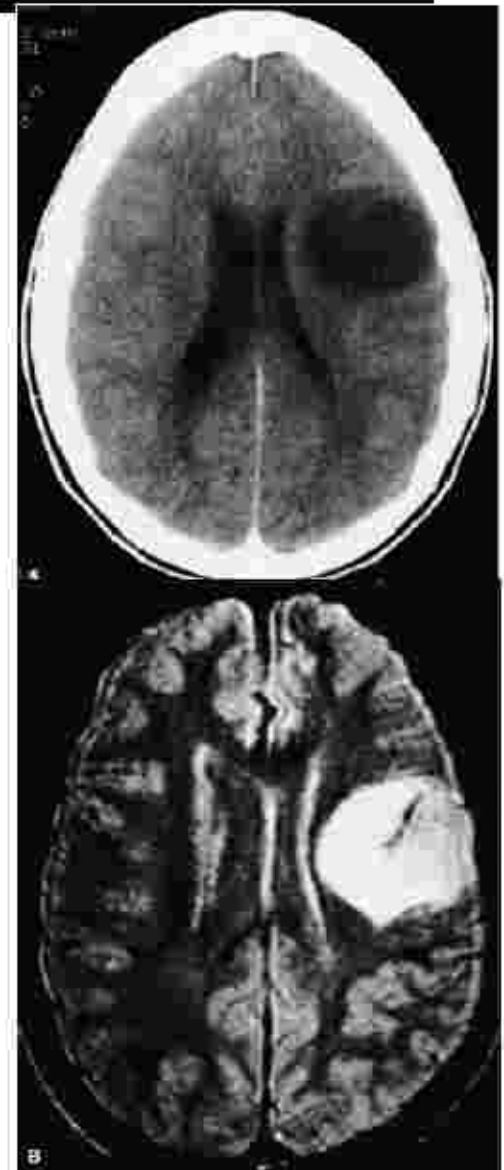
CTV: Phase I = GTV + 2.5 cm

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 + 1.5 cm

PTV: CTV + 0.5 cm