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: 0.8 cm
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
<table>
<thead>
<tr>
<th>n</th>
<th>GBM/AA</th>
<th>CT/MRI</th>
<th>Pathologic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>Not specified</td>
<td>CT</td>
<td>CT within 2 months of death; 29/35 tumors within 2 cm of the tumor mass on CT.</td>
</tr>
<tr>
<td>5</td>
<td>5/0</td>
<td>CT</td>
<td>In all cases neoplastic cells could be identified &lt; 3 cm from the periphery of the necrotic area on CT.</td>
</tr>
<tr>
<td>15</td>
<td>15/0</td>
<td>CT</td>
<td>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.</td>
</tr>
<tr>
<td>40</td>
<td>8/7</td>
<td>CT/MRI</td>
<td>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.</td>
</tr>
<tr>
<td>18</td>
<td>6/12</td>
<td>CT/MRI</td>
<td>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.</td>
</tr>
<tr>
<td>5</td>
<td>3/2</td>
<td>MRI</td>
<td>White matter edema on T2-MRI correlated 100% with tumor extension; MRI underestimated gray matter and subarachnoid space infiltration in three of five patients.</td>
</tr>
</tbody>
</table>
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: $PTV_1 = GTV + 0.5\, \text{cm}$; $PTV_2 = GTV + 1.5\, \text{cm}$; $PTV_3 = GTV + 2.5\, \text{cm}$ (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
Volume in relation to outcome (recurrence)

Table 6. Recurrence patterns at death

<table>
<thead>
<tr>
<th></th>
<th>Nonimplant arm [number (%)]</th>
<th>Implant arm [number (%)]</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original site (OS)*</td>
<td>64 (93)</td>
<td>38 (82)</td>
<td>122 (87)</td>
</tr>
<tr>
<td>OS + multifocal</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>OS + meningeal</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>OS + hematoogenous</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Other causes of death*</td>
<td>1</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Alive at time of analysis</td>
<td>4</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>71</td>
<td>140</td>
</tr>
</tbody>
</table>

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

Table 3. Patterns of failure

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

Lapperiere et al. JROBP 1998:41:1005
Souhami et al. JROBP 2004:60:853
# Volume in relation to outcome (recurrence)

<table>
<thead>
<tr>
<th>n</th>
<th>GBM/AA</th>
<th>Pre-/post-RT CT</th>
<th>Radiation treatment technique</th>
<th>Recurrence pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>1035</td>
<td>405/630</td>
<td>Post</td>
<td>WBI</td>
<td>95% of GBM and 91.4% of AA recurred at the site of the primary tumor</td>
</tr>
<tr>
<td>42</td>
<td>Not specified</td>
<td>Post</td>
<td>WBI</td>
<td>80% recurrence within 2 cm of enhancing mass; 10% partly within 2 cm</td>
</tr>
<tr>
<td>34</td>
<td>25/79</td>
<td>Pre</td>
<td>WBI: in 25 patients + come-down boost to 'tumor bed'</td>
<td>78% within 2 cm of enhancing edge on CT; 22% &gt; 2.0 cm</td>
</tr>
<tr>
<td>70</td>
<td>48/22</td>
<td>Pre</td>
<td>WBI + boost</td>
<td>72% within the boost field to enhancing mass plus 2 cm; 23% partly outside boost field; 93.7% (45 patients) had recurrence in radiation fields, i.e. contrast-enhancing mass plus 3 cm, in 48 patients, with follow-up CT</td>
</tr>
<tr>
<td>60</td>
<td>39/21</td>
<td>Pre</td>
<td>Seven patients WBI; 53 patients PBI</td>
<td>Majority of local recurrence at the primary site, i.e. zone of prolonged signal on T2-MRI plus 2.5–3.0 cm</td>
</tr>
<tr>
<td>66</td>
<td>Not specified</td>
<td>Pre</td>
<td>2 cm beyond enhancing mass</td>
<td>86% recurred in the PTV, i.e. contrast-enhancing mass plus 2 cm, in 58 patients, with recurrence documented by CT</td>
</tr>
<tr>
<td>36</td>
<td>23/13</td>
<td>Pre</td>
<td>Two patients WBI; 34 patients PBI</td>
<td></td>
</tr>
</tbody>
</table>
What should be the GTV, CTV and PTV for HGG?

- **RTOG:** Phase I: T2 +2.0 cm, Phase II: T1w contrast enhanced +2.5 cm
- **MRC:** T1w contrast + 3 cm (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