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

- Cavernous sinus
- Sphenoid sinus
- Optic chiasm
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 3-6 months after surgery or at any time later

- Imaging needs:
  - The narrower, the better (2 mm for SCRT) say 3 mm 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
  - 3-5 mm (or more) margin for PTV & 45 Gy/25 fx/5 weeks for all types
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 hypothalamic-pituitary damage
- Treatments:
  - Surgery (Biopsy, cyst drainage, partial removal or complete removal [mortality, morbidity, hypothalamic 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
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)

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

<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 2 cm 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.

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>58 (82)</td>
<td>122 (87)</td>
</tr>
<tr>
<td>OS + multifocal</td>
<td>0</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>OS + meningeal</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>OS + hematogenous</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>

Lapperriere et al. IJROBP 1998;41:1005

Souhami et al. IJROBP 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>25/9</td>
<td>Pre</td>
<td>WBI; in 25 patients + cone-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</td>
</tr>
<tr>
<td>60</td>
<td>39/21</td>
<td>Pre</td>
<td>Seven patients WBI; 53 patients PBI</td>
<td>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>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>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>
</tbody>
</table>
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 craniopharyngioma: 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.