Target Volume delineation

ICRU 62

GTV = Visible tumour and areas deemed to contain tumour

CTV = Microscopic extension

Internal Target Volume (ITV) = CTV + Internal margin (IM)

PTV = ITV + Set up margin (SM)
Imp points in Imaging for brain tumours

- CT scan alone should not be used, try to use MRI as well

- MRI – T1 contrast; T2/FLAIR sequences, thin slices, if preop MRI available- great for fusion; sag and coronal also, if possible

- 3D FSPGR sequence 1-3 mm slices with excellent resolution

- Equal matrix size (256x256), not oblique and equal spacing for MRI

- Important to check accuracy in CT/MRI fusion/co-registration (basilar artery, lens, IIIrd ventricle as common anatomical structures)

- Biological imaging
  - Magnetic Resonance spectroscopy (MRS)
  - Positron Emission Tomography (PET)
Important points before contouring

- Ensure high resolution planning scans, preferably with adequate contrast administration
- Review all pre-operative and post-operative scans in detail
- Good knowledge and experience in the tumour characteristics seen on radiology and anatomy
- When in doubt, discuss with the neurosurgeon and the radiologist
- High grade tumours (Gliomas, medullo, ependymoma), MUST do a post op scan within 24-48 hours
- For benign tumours, TREAT WHAT YOU SEE, so do a scan and plan RT 6-8 weeks post op.
Results after Surgery

After surgery alone, the regrowth rates are between 10 to 75%. RT reserved for large/invasive/recurrent cases.

<table>
<thead>
<tr>
<th>Study</th>
<th>Follow-up period</th>
<th>Recurrence rate after surgery (%)</th>
<th>Recurrence rate after surgery + RT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cicic et al., 1983 (7)</td>
<td>6 months–14 years</td>
<td>28</td>
<td>6</td>
</tr>
<tr>
<td>Ebersold et al., 1986 (8)</td>
<td>4 years–8 years</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td>Chun et al., 1988 (9)</td>
<td>2 years–18 years</td>
<td>19–22</td>
<td>2–10</td>
</tr>
<tr>
<td>McCollough et al., 1991 (11)</td>
<td>5 years–21 years</td>
<td>N/A</td>
<td>5</td>
</tr>
<tr>
<td>Comtois et al., 1991 (12)</td>
<td>1 year–16 years</td>
<td>21</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Radiotherapy

- Large residual disease
- Cavernous sinus invasion
- Suprasellar invasion
- Aggressive histology
- Recurrent tumours
Modern surgery – best cases

132 patients, 98 were advised postoperative observation

- no radiologic or surgical evidence of parapituitary invasion
- complete surgical removal
- absence of suprasellar extension
  2 months postoperatively
- no histologic feature of aggressive tumour behaviour (mitoses or poor cellular differentiation)

21 of 65 (32%) patients progressed at follow up of 20 years

Bradley Clin Endocrinol 1994
Need for RT?

Role of radiotherapy has been questioned

- Fear of RT complications
- Fear of increased morbidity for re-operations
- Lack of randomised data
- Will re-excise at recurrence (?morbidity/mortality)
- Better results with modern radiological and surgical techniques
Best non randomised data

**Comparative study of 2 surgical institutions; same RT set up**

<table>
<thead>
<tr>
<th></th>
<th>RT</th>
<th>No RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS</td>
<td>n=63</td>
<td>n=63</td>
</tr>
<tr>
<td>5 yr</td>
<td>93%</td>
<td>68%</td>
</tr>
<tr>
<td>10 yr</td>
<td>93%</td>
<td>47%</td>
</tr>
<tr>
<td>15 yr</td>
<td>93%</td>
<td>33%</td>
</tr>
</tbody>
</table>

Administration of RT was the only significant factor

Gittes C in Endocrinol 1998
RT in functioning tumours acromegaly

- Largest series of 884 patients with acromegaly treated with RT

- Mean GH levels declined from 13.5 ng/ml to
  - 5.3 ng/ml at 2 years
  - 2 ng/ml at 10 years
  - 1.1 ng/ml at 20 years

- 63% of patients achieved IGF-1 levels by 10 years
Pituitary adenoma
Cavernous sinus involvement
Immediate post op scan

Erich Steiner et al. Radiology 1992
Teng et al – AJNR 1988
Packing material / post operative changes

2 Mar 04

4 Mar 04
Sphenoid/Inferior extent uncommon but can happen
Late effects

- Hypopituitarism
- Optic Neuropathy
- Neurocognitive dysfunction
- Cerebrovascular Accidents
- Second Tumours
Stereotactic Conformal Radiotherapy

Accurate Immobilisation
Fractionated RT

Tight Conformation

Individualised planning

High Quality Assurance

Precise treatment delivery
French SRT data

110 consecutive patients treated with SRT to 50.4 Gy

75 with persistent macroscopic tumor, 47 with persistent hormonal secretions

Treated At minimum FU of 48 months, only 1 patient progressed (109/110 controlled/stable)

Of functioning adenomas, 42% had complete response and 100% had objective response

Probability of requiring hormonal replacement at 4 and 8 years: 28.5% and 35%

No other late sequelae
TMH audit of 3D CRT in pituitary adenomas

- Started in 2000

- 62 patients (48 non-functioning and 14 secretory)

- Carefully implemented protocol

- GTV: residual disease on planning scan

- CTV: 5mm margin, edited appropriately

- PTV: 5 mm margin three dimensionally as per departmental study of assessment of random and systematic errors
Seller tumours: 3DCRT with 3-4 field conformal non-coplanar

<table>
<thead>
<tr>
<th>Gantry</th>
<th>Table</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>260</td>
<td>350</td>
</tr>
<tr>
<td>20-50</td>
<td>90</td>
</tr>
</tbody>
</table>
Results of 3DCRT

- 34 females and 28 males

- Median follow up = 28 months (12 months to 62 months)

- All 62 patients had radiologically verified tumour control (3 year actuarial PFS 100%)

- Vision stable/improved in all patients

- 1 patient developed second tumour
Meningioma

MRI (post Gadolinium) - MUST

Dural tail sign
## Gross Total Resection: High Late Relapse

<table>
<thead>
<tr>
<th>Author</th>
<th>5-yr</th>
<th>10-yr</th>
<th>15-yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirimanoff (MGH)</td>
<td>7%</td>
<td>20%</td>
<td>32%</td>
</tr>
<tr>
<td>Condra (U Fl)</td>
<td>7%</td>
<td>20%</td>
<td>24%</td>
</tr>
<tr>
<td>Stafford (Mayo)</td>
<td>12%</td>
<td>25%</td>
<td>-</td>
</tr>
</tbody>
</table>

May sometimes cause significant morbidity in certain sites

References:
- Mirimanoff, Neurosurg 52:18, 1995
- Condra, UROBJ 39:427, 1997
### Subtotal Resection

<table>
<thead>
<tr>
<th>Author</th>
<th>5-yr</th>
<th>10-yr</th>
<th>15-yr</th>
<th>20-yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wara (UCSF)</td>
<td>47%</td>
<td>63%</td>
<td>-</td>
<td>75%</td>
</tr>
<tr>
<td>Condra (UFl)</td>
<td>47%</td>
<td>60%</td>
<td>70%</td>
<td>-</td>
</tr>
<tr>
<td>Stafford (Mayo)</td>
<td>39%</td>
<td>61%</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Condra, IJROBP 39:427, 1997
Adjuvant Radiotherapy
## 5 Yr Actuarial PFS

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>n</th>
<th>GTR</th>
<th>STR</th>
<th>STR+ RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirimanoff (1985)</td>
<td>225</td>
<td>93% (n=145)</td>
<td>63% (n=80)</td>
<td></td>
</tr>
<tr>
<td>Taylor (1988)</td>
<td>132</td>
<td>96% (n=90)</td>
<td>43% (n=42)</td>
<td>85% (n=13)</td>
</tr>
<tr>
<td>Glaholm (1990)</td>
<td>117</td>
<td></td>
<td></td>
<td>84%</td>
</tr>
<tr>
<td>Miralbell (1992)</td>
<td>115</td>
<td>48% (n=79)</td>
<td></td>
<td>88% (n=17, 8yPFS)</td>
</tr>
<tr>
<td>Mahmood (1994)</td>
<td>254</td>
<td>98% (n=183)</td>
<td>54% (n=65)</td>
<td>4/6 stable disease</td>
</tr>
<tr>
<td>Goldsmith (1994)</td>
<td>117</td>
<td></td>
<td></td>
<td>89% (98% p1980, n=77)</td>
</tr>
<tr>
<td>Condra (1997)</td>
<td>246a</td>
<td>95% (n=174)</td>
<td>83% (n=55)</td>
<td>86% (n=17, 5 atypical)</td>
</tr>
<tr>
<td>Stafford (1998)</td>
<td>581</td>
<td>88% (n=465)b</td>
<td>61% (n=116)</td>
<td></td>
</tr>
<tr>
<td>Nutting (1999)</td>
<td>82</td>
<td></td>
<td></td>
<td>92%</td>
</tr>
<tr>
<td>Vendrely (1999)</td>
<td>156</td>
<td></td>
<td></td>
<td>89% (12 &gt;WHO grade 1)</td>
</tr>
<tr>
<td>Dufour (2001)</td>
<td>31</td>
<td></td>
<td></td>
<td>93%</td>
</tr>
</tbody>
</table>

<p>| Total          | 2236 | 88-98%       | 43-83%       | 84-98%        |</p>
<table>
<thead>
<tr>
<th></th>
<th>PFS 2yrs</th>
<th>PFS 5yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtotal resection</td>
<td>44%</td>
<td>0%</td>
</tr>
<tr>
<td>STR + XRT</td>
<td>87%</td>
<td>0%</td>
</tr>
<tr>
<td>Total resection</td>
<td>70%</td>
<td>28%</td>
</tr>
<tr>
<td>TR + XRT</td>
<td>100%</td>
<td>57%</td>
</tr>
</tbody>
</table>

Meningiomas – Conformal RT

- Sharply delineated, Not infiltrating the brain, Complex shapes
- Often Adjacent to eloquent structures, 54 to 60 Gy required
Impact of modern RT planning

98%: RT with CT/MR (n=77)
77%: RT without CT/MR (n=40)

Progression-Free Survival
STR + postop RT; p=0.002

Fractionated Stereotactic/conformal radiotherapy

- Indicated for residual tumours
- Also for tumours close to critical structures such as optic apparatus/brain stem (optic sheath meningioma)
- 80-100% local control and PFS
- Less doses to the normal brain than conventional radiotherapy and so less toxicity
- Emerging impressive “prospective” data of maintained cognitive and neuropsychological function (Steinworth Radioth & Oncol 2003;69:177-82)

Debus IJROBP 2001
Jalali Clin Oncol 2002;14:103-9
Selch IJROBP 2004;59:101-11
Brain stem + spinal cord
NTCP organ models

Serial model (e.g. spinal cord, cranial nerves)

Any break causes complication, volume effect less important

Parallel Model (e.g. pituitary hypothalamic axis)
Damage a few - intact organ function, volume effect present
CTV generation

- Tumour histology; benign Vs low-grade Vs malignant
- Patterns of failure
- Resolution of neuro-imaging
- Confidence to delineate GTV accurately
- Any known anatomical barrier such as falx, tentorium, bone and base of skull
- Well studied and carefully implemented uniform margin generation protocol