General XRT Principles

- The most radioresistant tumor cell is the one that is out of the field.
- The worst complication is a local recurrence (unless you kill the patient with your treatment).

Conclusions

IMRT for lung cancer

- DON'T! Until......
  - Tumor motion can be taken into account
  - Dose calculation algorithms are better
  - The effects of low doses to large volumes of lung are better understood.

Conclusions

IMRT for lung cancer

- In the meantime......
  - Outline GTV as best as possible
  - Construct CTVs based on the literature
  - Construct PTVs based on measured tumor motion and known set-up uncertainty.

Problems with lung cancer

- Tumors biologically aggressive
  - Large tumors
  - Metastases
  - Inherently aggressive
- Surrounded by critical normal structures
  - Lung, esophagus, heart
- Tumors move
Problems with target definition

- GTV - tumor we see
  - GTV (primary) and GTV (nodes)
  - Windowing/leveling
  - Atelectasis
  - I.V. Contrast
- CTV - tumor we don’t see
  - How do tumors invade?

Problems with target definition

- PTV
  - Setup Uncertainty
  - Motion
    - 2D vs 3D motion measurement
    - ITV approach
    - Gating
- Don’t forget block edge!

Tumor volumes for 3D-CRT

cTV

- The tumor that you can see
  - GTV, for primary
  - GTV, for involved LN
- Primary must be outlined on pulmonary windows
- LN on mediastinal windows

Effect of Window/Level

- Lung Window (W1000/L-300)
- Mediastinal Window (W340/L25)
**FDG-PET scanning helps with GTV**
- metabolic activity
- Staging ~30% NSCLC upstaged (MacManus)
- Can reduce contour variation (Caldwell)
- Can dramatically affect radiation planning
- BUT: PET very bad at edges!
- Be wary of stage migration - PET staged patients have MS≈31 months!

**Tumor volumes for 3D-CRT**

PET (14) vs. CT (29) meta-analysis

<table>
<thead>
<tr>
<th></th>
<th>PET</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>.79</td>
<td>.60</td>
</tr>
<tr>
<td>Specificity</td>
<td>.91</td>
<td>.77</td>
</tr>
<tr>
<td>Positive PV</td>
<td>90%</td>
<td>50%</td>
</tr>
<tr>
<td>Negative PV</td>
<td>93%</td>
<td>85%</td>
</tr>
</tbody>
</table>

Dwamena, et al., Radiology 213:530, 1999
**PET-CT Proposed guidelines**

- **Atelectasis**
  - SUV > 2.5 with 1 cm margin - still GTV!
  - Not across anatomic boundaries

- **Nodes**
  - Use to identify nodes on scan
  - Don’t draw GTV on PET!!!
  - If no nodes in PET positive area
    - check registration, then use clinical judgement

**Tumor volumes for 3D-CRT CTV**

- Where the tumor might be
  - CTV₁
    - microscopic extension of primary
  - CTV₂
    - microscopic nodal disease

**Tumor volumes for 3D-CRT CTV₁**

- 354 slides from 70 patients
- Adeno 2.48 ± 2.55 (0-12mm)
- Squam 1.09 ± 2.00 (0-13mm)

- Therefore 8mm and 6mm margin
- Would have missed 5/176 and 4/178
- Caveat: lungs not inflated before fixation

**Tumor volumes for 3D-CRT CTV₂**

- Where the tumor might be
  - CTV₂
    - microscopic nodal disease
    - ????

**PTV Setup Uncertainty**

- Our observations
  - symmetrical
  - 1 s.d. = 3.5 mm
  - more immobilization better (alpha cradle and wing board)
    - (1 s.d. = 5 mm with just alpha cradle)

**PTV Motion**
Tumor motion not predictable
- size, location, PTV
Motion is complex
- hysteresis
Patients breath differently day-to-day
Patients breath differently at start and end
Normal tissues move too

2D vs 3D
- 22 patients studied on double exposure CXR
- SI tumor motion 4.5±5.0 (8-22mm)
  - 12 moved, 10 did not

Arrows denote tumor motion

SI tumor motion was not predictable

<table>
<thead>
<tr>
<th>Position</th>
<th>Mean ± std (mm)</th>
<th>Size (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertex</td>
<td>3.5 ± 7.1 (0.4-37)</td>
<td>9.9</td>
</tr>
<tr>
<td>Center</td>
<td>2.0 ± 13.1 (0-37.1)</td>
<td>0.18</td>
</tr>
<tr>
<td>Lobe</td>
<td>4.0 ± 13.1 (0-37.1)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Protocol ID00-202 (CS-PI, KF-CT, HL-MRI)
CT arm of this protocol
- Acquire CT image sets at fixed levels of inspiration: DIBH (60% Vc), 100% TV, end expiration (0% TV)
- The vector difference in tumor centroid position between 100% and 0% TV should represent the motion during normal respiration
The Vector difference in position motion from expiration to inspiration.
Lung tumors aren’t bricks

What variables predict for motion?

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>STD</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1/T2</td>
<td>9.5</td>
<td>4.2</td>
</tr>
<tr>
<td>T3/T4</td>
<td>8.4</td>
<td>4.7</td>
</tr>
<tr>
<td>Upper</td>
<td>7.8</td>
<td>3.6</td>
</tr>
<tr>
<td>Lower</td>
<td>12.9</td>
<td>3.9</td>
</tr>
<tr>
<td>Free</td>
<td>12.4</td>
<td>3.4</td>
</tr>
<tr>
<td>Attached</td>
<td>7.8</td>
<td>3.9</td>
</tr>
</tbody>
</table>

MOTION change in the R-L direction

Change in A-P Motion

Motion change in I-S direction
Tumor volumes for 3D-CRT

ICRU 62
- ITV = CTV + IM
- ITV + SM (setup margin) = PTV

Internal Target Volume

How do we determine ITV?
1. Gating device (long acquisition times)
2. Use a spirometer system
   - Acquire CT scans at shallow breathing
   - Acquire CT about lesion at
     - 60% VC
     - 30% VC
     - 0% Tidal volume

Flow
Mouth Pressure
Volume

Flow / Pressure (l/s / cm H₂O)
Gating

- Why gate treatment?
  - We can treat tumor with ITV, so…
- Gating is to reduce irradiation of lung!!

Treatment planning

- CT data sets and contours transferred to Pinnacle
- CTVs generated by uniform 0.8 cm expansion of GTVs
- Define ITV to be envelope of CTV 0 and CTV 100

Treatment planning

- PTV ITV generated by uniform 1.0 cm expansion of ITV – setup uncertainty, motion uncertainty
- PTV 0.7 generated by uniform 0.7 cm expansion of CTV 0 - setup uncertainty, no gating uncertainty

Dose calculations

- All calculations done on free-breathing data set
- Ideally, compute PTV ITV plan on free-breathing data set, PTV 0.7
- CT data sets acquired at different times
- Somewhat different geometries
Dose calculations

- Keep comparisons uniform by using same data set
- Set uniform densities:
  - ITV = 0.7
  - Lung = 0.3

Assess potential lung morbidity

- Compute DVH for total lung
- Record V20 for total lung
- Record mean total lung dose

Data analysis

- Compute GTV excursion
  - center of circumscribing box
- Compute V20 ratios and mean dose ratios between gated and ITV plans
  - PTV 0.7 and PTV ITV plans

Results

- Does not appear to be correlation between GTV displacement and V20 ratio for 0.7 cm PTV margin
- But – look at V20 ratio as function of GTV volume
Results

- For 5 out of 7 cases where GTV volume > 100 cm³, V20 ratio greater than 0.95 – little benefit to be gained by gating
- Remove cases for which GTV volume > 100 cm³ from analysis

Conclusions

- Gating can reduce the amount of irradiated uninvolved lung
  - For GTV < 100 cm³
  - For GTVs that exhibit significant excursion (1 cm³)
  - Provided there is little uncertainty as to the location of the tumor during gating

Tumor volumes for 3D-CRT

- A variety of techniques used.
  - Spirometry (ABC vs DIBH)
  - Chest wall motion
- They are time consuming
- Until this issue is resolved, use ITV

ITV

- Advantages
  - Do not miss tumor!
  - No special equipment or techniques
- Disadvantages
  - May treat slightly more volume
  - Dosimetry not quite correct
A word about heterogeneity

- It is safe to use heterogeneity corrections
  - isocontor dose about the same
  - better target volume coverage
- If you don’t use heterogeneity corrections
  14/30 pts delivered less than 90% of the prescription dose to PTV
  tempted to use >10MV beams

Comparison of Dosimetry Algorithms:
6 MV Broad Beam Broad Target

Photon Monte Carlo
EGS4/MCDOSE

Comparison of Dosimetry Algorithms:
6 MV IMRT Beamlet Broad Target

Photon Monte Carlo
EGS4/MCDOSE

Perez and Brady, 1997
**Lung IMRT (primary)**

**Wedge-Pair**

**Conventional**

**6MV 96MV 9--Field**

**Conclusion**

**IMRT for lung cancer**

- Tumor motion can be taken into account
- Dose calculation algorithms are better
- The effects of low doses to large volumes of lung are better understood.

**Conclusions**

**IMRT for thoracic tumors**

- Mesothelioma
- Superior sulcus
- Esophagus
Mesothelioma Isodose Distributions

50 Gy

30 Gy