ADJUVANT RADIOTHERAPY - CARCINOMA LUNG

Prof Ramesh S Bilimagga
President AROI
Group Medical Director - HCG
ADJUVANT THERAPY

Additional cancer treatment given after primary treatment to control the microscopic disease in order to lower the risk of recurrence.

National Cancer institute
A page from a presentation slide listing different types of cancer therapy:

- Radiation therapy
- Chemotherapy
- Hormone therapy
- Biological therapy
- Combination any of the above
WHY ADJUVANT

- NSCLC constitutes 80% of Lung cancer
  - 30% complete surgical resection
  - long term survival.
- Post Surgery Recurrence rates
  - STAGE I - 20%
  - STAGE IIIA - 50%
- Intra thoracic recurrence
  - Along surgical stump
  - Mediastinal lymph nodes
Chemotherapy and Radiotherapy evaluated to improve prognosis.

High rate of local failure after surgery & Post op Chemo
- New interest on PORT came into picture.
SURGERY IN CA LUNG

- Wedge Resection
- Segmentectomy
- Lobectomy
- Pneumonectomy
INDICATIONS - PORT

- Stage I & II – close/positive margins.

- Stage IIIA
  - Close margin (<5mm),
  - Positive margin,
  - N2 disease,
  - Nodal ECE.
RT PLANNING

- Immobilization
- Simulation scan
- Transferring images to planning system
- Contouring
- Dose constraints to both target and OAR’s
- Plan approval
- Daily verification of treatment setup
- Plan execution
- Weekly review
IMMOBILIZATION
Supine position
Spine straight
Hands above the head
Lasers aligned
Orfit cast
Contrast+/–
Serial CT
Thickness <5mm
# Mediastinal Lymph Nodes

**Superior Mediastinal Nodes**
- **1** Highest Mediastinal
- **2** Upper Paratracheal
- **3** Pre-vascular and Retrotracheal
- **4** Lower Paratracheal (including Azygos Nodes)

*Subscripts:*
- $N_1$: single digit, ipsilateral
- $N_2$: single digit, contralateral or supraclavicular

**Aortic Nodes**
- **5** Subaortic (A-P window)
- **6** Para-aortic (ascending aorta or phrenic)

**Inferior Mediastinal Nodes**
- **7** Subcarinal
- **8** Paraesophageal (below carina)
- **9** Pulmonary Ligament

**$N_1$ Nodes**
- **10** Hilar
- **11** Interlobar
- **12** Lobar
- **13** Segmental
- **14** Subsegmental
CTV for right lung cancers includes bronchial stump and LN stations 2R, 4R, 7, and 10 To 11R.
CTV for left lung cancers includes bronchial stump and LN stations 2R, 2L, 4R, 4L, 5, 6, 7, and 10 To 11R.
LRF sites in left- and right-sided lung cancers are shown. The proposed PORT fields for left- and right-sided lung cancers are presented. Solid star symbols are multiple-site failures (patients failing in multiple LRF sites simultaneously); open star symbols are isolated failures (patients with a single LRF site). For patients with left-sided tumors, all LRF would have been covered by the proposed PORT CTV. For patients with right-sided tumors, 83% (39 of 47) LRF would have been contained in the PORT field; 17% (8 of 47) LRF were outside the proposed PORT field and observed in 6 patients ( ). CTV = clinical tumor volume; LRF = local-regional failure; PORT = postoperative radiation therapy.
CTV to include
- Positive margin or microscopic extension disease.
- Surgical clips in positive margin Stage 1 & 2

PTV – 1cm around CTV

3D CRT will improve the loco regional control rate compared to 2D.
STATUS OF LUNG PORT

- No clear cut consensus on definition of the extent of CTV

- After PORT meta analysis (1998) PORT in ca lung banned in many RT departments world wide.
PORT RESULTS RATIONALE

- In the previous trials most of the patients with stage I & II with NO/N1 were also included which showed detrimental effect.

- But for N2 patients there was no clear adverse effect.

- So the trials mainly started for those patients with N2 disease.
**Review of Literature**

<table>
<thead>
<tr>
<th>Study</th>
<th>Stage</th>
<th>n of patients</th>
<th>Dose (Gy)</th>
<th>Local recurrence (%)</th>
<th>Overall survival (%)</th>
<th>Follow-up method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astudillo and Connill</td>
<td>IIIA</td>
<td>60</td>
<td>–</td>
<td>20%</td>
<td>28%</td>
<td>3-yr actuarial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>86</td>
<td>45–50</td>
<td>13%</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Green et al.</td>
<td>I–IIIA</td>
<td>94</td>
<td>–</td>
<td>NR</td>
<td>16%</td>
<td>5-yr crude</td>
</tr>
<tr>
<td></td>
<td></td>
<td>125</td>
<td>50–60</td>
<td>NR</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Choi et al.</td>
<td>IIIA</td>
<td>55</td>
<td>40–56</td>
<td>31%</td>
<td>8%</td>
<td>5-yr actuarial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>93</td>
<td></td>
<td></td>
<td>43%</td>
<td></td>
</tr>
<tr>
<td>Chung et al.</td>
<td>I–IIIA</td>
<td>68</td>
<td>–</td>
<td>32%</td>
<td>28%</td>
<td>3-yr crude</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>46</td>
<td>10%</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>Paterson et al.</td>
<td>T3N0–2</td>
<td>22</td>
<td>–</td>
<td>27%</td>
<td>30%</td>
<td>5-yr actuarial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13</td>
<td>20–50</td>
<td>0</td>
<td>56%</td>
<td></td>
</tr>
<tr>
<td>Kirsh et al.</td>
<td>IIIA</td>
<td>20</td>
<td>–</td>
<td>NR</td>
<td>0%</td>
<td>5-yr crude</td>
</tr>
<tr>
<td></td>
<td></td>
<td>110</td>
<td>50–60</td>
<td>NR</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>Sawyer et al.</td>
<td>IIIA</td>
<td>136</td>
<td>–</td>
<td>60%</td>
<td>22%</td>
<td>4-yr actuarial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>88</td>
<td>45–66</td>
<td>17%</td>
<td>43%</td>
<td></td>
</tr>
</tbody>
</table>

*Risk of local recurrence lower with PORT (25%-35%) based on the above results*
Randomized trials showing the results of with / without PORT

<table>
<thead>
<tr>
<th>Study</th>
<th>Stage</th>
<th>n of patients</th>
<th>Total dose/ fraction size</th>
<th>LRR (%)</th>
<th>p</th>
<th>5-yr SR (%)</th>
<th>p (in favor)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Houtte et al. 1980</td>
<td>T1–3N0</td>
<td>104</td>
<td>–</td>
<td>10.9%</td>
<td>NS</td>
<td>43%</td>
<td>&lt;.05 (surgery)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>98</td>
<td>60/2 Gy</td>
<td>1.2%</td>
<td>NS</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Lung Cancer Study Group 1986</td>
<td>II–III SCC</td>
<td>120</td>
<td>–</td>
<td>41%</td>
<td>.001</td>
<td>40%</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>110</td>
<td>50.4/1.8</td>
<td>3%</td>
<td></td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>Dautzenberg et al. 1999</td>
<td>I–II–III</td>
<td>355</td>
<td>–</td>
<td>28%</td>
<td>NS</td>
<td>43%</td>
<td>.002 (surgery)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>373</td>
<td>60/2–2.5</td>
<td>22%</td>
<td></td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Mayer et al. 1997</td>
<td>I–II–III</td>
<td>72</td>
<td>–</td>
<td>20%</td>
<td>&lt;.01</td>
<td>20.4%</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>83</td>
<td>50–56/2</td>
<td>7%</td>
<td></td>
<td>29.7%</td>
<td></td>
</tr>
<tr>
<td>Trodella et al. 2002</td>
<td>T-2N0</td>
<td>53</td>
<td>–</td>
<td>23%</td>
<td>.19</td>
<td>58%</td>
<td>.048 (PORT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51</td>
<td>50.4/1.8</td>
<td>2.2%</td>
<td></td>
<td>67%</td>
<td></td>
</tr>
<tr>
<td>Feng et al. 2000</td>
<td>II–III</td>
<td>182</td>
<td>–</td>
<td>33.2%</td>
<td>.01</td>
<td>40.5%</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>183</td>
<td>60/2</td>
<td>12.7%</td>
<td></td>
<td>42.9%</td>
<td></td>
</tr>
</tbody>
</table>

*aCumulative rate of local recurrences.
*bStudy not included in the meta-analysis published in 1998.
Abbreviations: LRR, local recurrence rate; NS, nonsignificant; PORT, postoperative radiation therapy; SCC, squamous cell carcinoma; SR, survival rate.
SEER (JCO 2006)

- 7,400 patients, stage II–III NSCLC post op + PORT

- T3-T4 advanced nodal stage
  - Involved vs Sampled ratio of Lymphnodes

- On multivariate analysis
  - Older age T3,T4 N2 stage male,
  - Fewer sampled LN greater no of LN involved had negative impact on survival.

- 5-year OS for
  - N2 patients (20→27%, HR 0.85)
  - N0 (41 → 31%, HR 1.2)
  - N1 (34 → 30%, HR 1.1)
PORT META-ANALYSIS TRIALIST GROUP

- 2128 patients.
- 9 randomised trials of PORT vs Sur
- 21% relative increase in the risk of death with RT
- 2 yr reduced OS from 55% to 48%
- Adverse effect was greatest for Stage I,II
- St.III (N2): no clear evidence of an adverse effect

Lancet 1998;352:257
PORT TRIALS

- Postoperative RT should be used outside of a clinical trial in Stage I, II lung cancer when surgical margins are positive and repeated resection is not feasible.
VAN HOUTTE ET AL (1980):

- NSCLC Stage I–II
- Observation vs Post-op 60Gy to mediastinum.
- RT improved local-regional control,
- 5-year OS 24% RT vs. 43% with observation
- Increased pneumonitis.
- Study criticized because used Co-60 machines, large field size, and no CT planning.
ANITA TRIAL
(ADJUVANT NAVELBINE INTERNATIONAL TRIALIST ASSOCIATION)

- Post op adjuvant chemo or observation and RT was not randomised but decided before initiation of study.
- RT dose 45-60Gy at 2Gy/#

<table>
<thead>
<tr>
<th>MEDIAN SURVIVAL</th>
<th>pN1 patients</th>
<th>pN2 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WITH OUT RT</td>
<td>WITH RT</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>93.6m</td>
<td>46.6m</td>
</tr>
<tr>
<td>Observation</td>
<td>25.9m</td>
<td>50.2m</td>
</tr>
</tbody>
</table>
ECOG – 3590 TRIAL

- 488 pt’s
- Stage II - IIIA NSCLC post op negative margins.
- RT Vs CT+RT
- Result – No difference in LC or survival.
RTOG 9705 TRIAL – PHASE 2

- 88 pt’s
- Stage II to IIIA NSCLC post operative CT+RT
- CT- carboplatin + paclitaxel
- RT – 50.4Gy/28Fr
- + Boost 10.8Gy/6Fr for Extra nodal extension or T3 lesions.
Median F/U 56.7 months. Median OS 56.3 months

<table>
<thead>
<tr>
<th>Year</th>
<th>OS</th>
<th>PFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1Y</td>
<td>86%</td>
<td>70%</td>
</tr>
<tr>
<td>2Y</td>
<td>70%</td>
<td>57%</td>
</tr>
<tr>
<td>3Y</td>
<td>61%</td>
<td>50%</td>
</tr>
</tbody>
</table>

RTOG conclusion- with acceptable toxicities there might be improvement in OS & PFS with chemoradiotherapy in resected NSCLC pt’s.
PATTERNS OF FAILURE

- Rt lung – ipsilateral superior Mediastinal nodes.
- Lt Lung - bilateral superior Mediastinal nodes.

- Mediastinal CTVs
  - Involved LN’s & a margin corresponding to the upper and lower LN’s to the involved LN area and all LN’s lie between two noncontiguous involved LN’s.
TREATMENT TECHNIQUES
Target can be seen and contoured.

Coverage can be assessed to the target.

Dose to the OAR’s can be verified and if required can be optimized by changing the weightage to the beams.
IM-IGRT

- Target coverage will be better at the same time the OAR’s can be spared better than 3D-CRT.

- Daily verification can be done by either KVCT/MVCT image, which will improve the accuracy of treatment and reduces the chances of random errors.
DOSES

- If R0 resection - 50-56 Gy / 25-28#
- If N2 with ECE - 10-16 Gy boost.
- If positive margin - 60 Gy / 30#
- If gross residual disease - 66-70 Gy / 33-35#

along with concurrent chemo.
Conclusions

- Radiotherapy is a proven adjuvant therapy in Stage 1, 2 (+ margin) & 3A
- IM-IGRT > 3D CRT > 2D treatment
- Volume delineation is of prime importance
THANK YOU