Radiotherapy in Lung

Cancer Anatomy

- Oblique fissure in both lungs.
- Horizontal fissure in Right lung.
- Trachea bifurcates at the level of T5.
- Lymph nodes are divided into stations.
- Intrapulmonary, bronchopulmonary (hilar), mediastinal, suprACLavicular (scalene) nodes.
**Superior Mediastinal Nodes**
- 1 Highest Mediastinal
- 2 Upper Paratracheal
- 3 Pre-vascular and Retrotracheal
- 4 Lower Paratracheal (including Azygos Nodes)

*Note: N₂ = single digit, ipsilateral
N₃ = 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

**N₁ Nodes**
- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental
- 14 Subsegmental
Epidemiology

- Most common & Deadliest worldwide.
- Survival at 5 years in USA is 15%.
- Primary risk factor- SMOKING (~90%) • Adenocarcinoma more than Small/Squamous.
  (Filtered cigarette, fine particles reach periphery)

Presentation

- Due to local tumor growth:
  - Centrally cough, haemoptysis, obstructive signs.
  - Peripherally silent, cough, pleuritic chest pain.
- Nerve entrapment (LRLN, phrenic), Vascular obstruction.
- Esophageal narrowing, obstruction, fistula.

- Due to metastasis:
  - 60% SCLC, 30% - 40% NSCLC.
  - CNS, Bones, Liver, Adrenal Glands.

Workup

- History:
  - Smoking, Weight loss, Performance status ● Examination ● Imaging:

  - CECT incl. adrenals, PET-CT preferred.(50\% staging changed)
  - CECT (sens 75%, spec 66\%) vs PET-CT (91\%, 86\%)
  - EBUS
● Tissue:
  – FNAC, TBFNA, Mediastinoscopy, VATS
## TABLE 1: TNM staging of lung cancer

### Primary tumor (T)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tx</td>
<td>Tumor proven by the presence of malignant cells in bronchopulmonary secretions but not visualized roentgenographically or bronchoscopically or any tumor that cannot be assessed, as in pretreatment staging</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor ≤ 3.0 cm in greatest dimension, surrounded by lung or visceral pleura, and without evidence of invasion proximal to a lobar bronchus at bronchoscopy</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor &gt; 3.0 cm in greatest dimension; or tumor of any size that either invades the visceral pleura or has associated atelectasis or obstructive pneumonitis extending to the hilar region (but involving less than the entire lung). At bronchoscopy, the proximal extent of demonstrable tumor must be within a lobar bronchus or at least 2.0 cm distal to the carina</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor of any size with direct extension into the chest wall (including superior sulcus tumors), diaphragm, or mediastinal pleura or pericardium without involving the heart, great vessels, trachea, esophagus, or vertebral body; or tumor in the main bronchus within 2 cm of, but not involving, the carina</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor of any size with invasion of the mediastinum or involving the heart, great vessels, trachea, esophagus, vertebral body, or carina; or presence of</td>
</tr>
</tbody>
</table>

### Regional lymph nodes (N)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nx</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No demonstrable metastasis to regional lymph nodes</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis to lymph nodes in the peribronchial and/or ipsilateral hilar region, including direct extension</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis to ipsilateral mediastinal and subcarinal lymph nodes</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis to contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph nodes</td>
</tr>
</tbody>
</table>

### Distant metastasis (M)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mx</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

### Stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>T3</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
Overview of management in NSCLC

- Surgery is the main stay for resectable and operable non small cell lung cancer
- Radiation plays a role in the definitive and adjuvant management of NSCLC
- Chemotherapy is an important adjuvant treatment modality, often used with radiation
- Radiation along with chemotherapy are useful for palliation

RT in Lung Cancer: Issues

- NSCLC: A moderately radio-sensitive tumor: dose escalation needed
- Surrounded by organs which are dose limiting: heart, opp. lung, spinal cord, esophagus
- Respiratory motion: a pertinent factor necessitating motion management in radiation delivery
RT in NSCLC: Stage wise

- Stage: I: Surgery the mainstay; SBRT
- Stage II: Surgery the mainstay; SBRT
- Stage III: Surgery + RT, CT + RT
- Stage IV: Palliative RT
- Prophylactic cranial irradiation*
Adjuvant Radiation Therapy

- Indicated for insufficient margins* <1cm, mediastinal nodes (N2).
- 60-66Gy, 2Gy/# to the positive margin. 50 Gy/25# to probable microscopic disease.
- PORT Meta analysis 21% more risk of death in post operative RT group.

- Studies since 1965, unpublished data included, ill-defined surgical techniques, 7 of 9 trials used Co-60 unit, Crude technology of radiation therapy
Early stage NSCLC

• Surgical resection: well established as the main curative treatment in stage I, II NSCLC
• 5-year overall survival for (p) stage I disease: 57% to 67%
• Poor PS, medical comorbidities & often preference preclude surgery in a large proportion (25%*)
• 5-year survival rates with unresectable stage I, II disease treated with radiotherapy range from 15% to 30%.
• 60% death due to distant metastasis

• Lancet Oncol 2009; 10: 885–94
• Better results with dose escalation.
• Difficult to achieve with conventional radiation delivery techniques
• Options now available:
(A) SBRT / Cyber knife

(B) Real time motion management: IGRT

(C) Brachytherapy: endoluminal and interstitial

Patient selection criteria for SBRT in early stage NSCLC

- Medically inoperable or don't want surgery
- PS 0-2
- Stage T1-3, N0 following PET-CT
- Maximum tumor size 5cm
- Not adjacent to major structures like vessels, heart, esophagus.
- Able to lie flat for at least one hour

SBRT vs Wedge resection in Stage I NSCLC

- 124 pts; T1-2N0MO
- 69 wedge resections, 58 SBRT
• SBRT prescribed as 48(T1) or 60(T2) Gy in 4 to 5 fractions
• Median follow up of 2.5 years
• No differences in DM, FFF, or CSS, but OS was higher with wedge resection at 30 months. (87% vs 72%)

(Distant Metastasis, Freedom from Failure, Case Specific Survival)

Brachytherapy for early stage NSCLC

- Endobronchial (endoluminal) brachytherapy
- Interstitial brachytherapy
  NSCLC : Definitive RT
Stage III:
- Main bulk of the disease.
- 60 – 75 Gy to the gross disease (RTOG 73-01)
- 50 Gy to the microscopic disease – Hyperfractionation showed better roles.
- 69.6 Gy. 1.2Gy/#, 2#/day.

Best survival rates (20% at 3 years)
- CHART (Continuous Hyperfractionated Acclerated Radiotherapy) : 1.5Gy/#. 3#/day. 36#. Total: 54Gy
- RT vs CT/RT Benefit: 2 months (at 3 years)


RT Techniques: 2D Planning

- 2 cm margin around any gross tumor.
- 1 cm margin around regional LN groups.
• Upper lobe tumor: B/L supraclav & subcarina.
• Middle lobe tumor: Entire mediastinum (thoracic inlet to 8 cm below carina)
• Lower lobe tumor: Entire mediastinum from thoracic inlet to diaphragm.
RT Techniques: 3DCRT

- CT Scan in treatment position. (optional Styrofoam)
- GTV: primary tumor & any gross lymph nodes.
- CTV: Area thought to harbor micrometastasis (hilar / mediastinal LN, Margin).
- PTV: Margin for physiologic organ motion during treatment and daily inaccuracies.
• Visible tumor by any imaging modality.
• Pulmonary extent: on pulmonary windows. ● Mediastinal extent: mediastinal windows.
• Lymph node >1 cm in shortest: +ve (15% chance)
• FDG-PET: quite important. (collapse vs tumor, LNs)
CTV

- Contains gross and microscopic disease.
- GTV-to-CTV: 6 mm for squamous cancers 8 mm for adenocarcinomas to cover the gross tumor and microscopic disease with 95% accuracy. For others, 8mm.
- In the absence of radiographic proof of invasion, CTV of primary lesion should not extend into the chest wall or mediastinum.
- CTV expansions of lymph node disease should not extend into the major airways or lung.


PTV
• CTV + margin for daily setup error and target motion.
• 4D CT study, 50% of the tumor moves > 5 mm
  13% moves > 1 cm (more when near diaphragm)
• Individual assessment is recommended.
• Breath holding, Gated techniques.
• ITV: Only takes the organ movements.

ICRU 62
Dose and volume

- Gross disease i.e. primary and involved nodes: 65-70 Gy (+/- CT)
- Elective nodal irradiation not recommended
More radiation pneumonitis with ENI (29% vs. 17%, P = 0.044).
<table>
<thead>
<tr>
<th>Structure</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>Both lungs should be contoured using pulmonary windows. The right and left lungs can be contoured separately, but they should be considered as one structure for lung dosimetry. All inflated and collapsed, fibrotic and emphysematic lungs should be contoured, small vessels extending beyond the hilar regions should be included; however, GTV, hilars and trachea/main bronchus should not be included in this structure.</td>
</tr>
</tbody>
</table>
Heart

The heart will be contoured along with the pericardial sac. The superior aspect (or base) will begin at the level of the inferior aspect of the pulmonary artery passing the midline and extend inferiorly to the apex of the heart.

<p>| Esophagus     | The esophagus should be contoured from the beginning at the level just below the cricoid to its entrance to the stomach at GE junction. The esophagus will be contoured using mediastinal window/level on CT to correspond to all muscular layers out to the fatty adventitia. |</p>
<table>
<thead>
<tr>
<th>Section</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinalcord</td>
<td>The spinal cord will be contoured based on the bony limits of the spinal canal. The spinal cord should be contoured starting at the level just below cricoid (base of skull for apex tumors) and continuing on every CT slice to the bottom of L2. Neuro foramenines should not be included.</td>
</tr>
<tr>
<td>Brachial plexus</td>
<td>This is only required for patients with tumors of upper lobes. Only the ipsilateral brachialplex is required. This will include the spinal nerves exiting the neuro foramine from top of C5 to top of T2.</td>
</tr>
</tbody>
</table>

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## Dose-Volume Constraint

<table>
<thead>
<tr>
<th>Organ</th>
<th>RT Alone</th>
<th>Chemo/RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cord</td>
<td>50 Gy</td>
<td>45 Gy</td>
</tr>
<tr>
<td>Lung</td>
<td>MLD &lt;20 Gy</td>
<td>MLD &lt;20 Gy</td>
</tr>
<tr>
<td></td>
<td>V20 &lt;40%</td>
<td>V20 &lt;35%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>V10 &lt;45%</td>
</tr>
<tr>
<td>Heart</td>
<td>V40 &lt;50%</td>
<td>V40 &lt;50%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Dmax &lt;75 Gy</td>
<td>Dmax &lt;75 Gy</td>
</tr>
<tr>
<td></td>
<td>V60 &lt;50%</td>
<td>V55 &lt;50%</td>
</tr>
<tr>
<td>Tissue</td>
<td>Dose Requirements</td>
<td>Institution</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Kidney</td>
<td>20 Gy (&lt;50% of combined both kidneys or &lt;75% of one side of kidney if another</td>
<td>Same as RT</td>
</tr>
<tr>
<td></td>
<td>kidney is not functional)</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>30 Gy (&lt;40%)</td>
<td>Same as RT</td>
</tr>
</tbody>
</table>

**IMRT**

- Dose escalation without big dose to surrounding tissue.
- Benefits in Prostate and Head & Neck.
- Scientists were skeptical about IMRT in Lungs due to assumption that IMRT may deliver low yet
damaging doses to a larger volume of normal lung tissue.

- Movement of a tumor because of respiration introduces another level of complexity to both the IMRT dosimetry and the technique used.

**IMRT**

- Found that IMRT may be more suitable than 3D CT treatment planning for cases of advanced-stage disease with a larger GTV.

- Median absolute reduction of lung volume irradiated above 10 and 20 Gy were 7% and 10%, respectively.
• >2 Gy less mean total lung dose and 10% decrease in the risk of radiation pneumonitis.
• Heart, Esophagus, thoracic tissue dose decreased.


IMRT

- Tumors in the superior sulcus or close to the esophagus or spinal cord or patients with positive lymph nodes may benefit more.
- Earlier-stage, small mobile tumors may not be good candidates for IMRT
Proton Beam

- Well-defined range of penetration.
- By modulating the Bragg peak across the target volume, proton beams can deliver a full, localized, uniform dose of energy to the treatment site while sparing the surrounding normal tissues.
- In combination with IGRT.
- Results comparable to surgery in stage IA.
Spread out Bragg Peak
Palliative Radiotherapy

- Stage IIIB/IV
- 40Gy/20# vs 30Gy/10# → No difference.
- 20Gy/10# for short term palliation.
<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Stage/Performance</th>
<th>Dose, Gy</th>
<th>Fractions</th>
<th>Survival, Months</th>
<th>Symptom response/comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simpson et al, 1985\textsuperscript{23}</td>
<td>409</td>
<td>Inoperable, stage IIIB</td>
<td>30</td>
<td>10</td>
<td>6</td>
<td>Overall 69%/No difference between the 3 arms</td>
</tr>
<tr>
<td>Teo et al, 1988\textsuperscript{24}</td>
<td>291</td>
<td>Inoperable</td>
<td></td>
<td></td>
<td>6</td>
<td>71% (P = .02)</td>
</tr>
<tr>
<td>MRC, 1991\textsuperscript{25}</td>
<td>369</td>
<td>Mostly stage IIA or IIIB</td>
<td>31.2</td>
<td>4</td>
<td>5</td>
<td>54%</td>
</tr>
<tr>
<td>MRC, 1992\textsuperscript{26}</td>
<td>235</td>
<td>Inoperable/Poor performance</td>
<td>17</td>
<td>2</td>
<td>3</td>
<td>65--81%</td>
</tr>
<tr>
<td>Abratt et al, 1995\textsuperscript{27}</td>
<td>84</td>
<td>Unresectable/WHO 0-1</td>
<td>35</td>
<td>10</td>
<td>8.5</td>
<td>48--75%</td>
</tr>
<tr>
<td>Macbeth et al, 1995\textsuperscript{28}</td>
<td>509</td>
<td>Inoperable, nonmetastatic/Good performance</td>
<td>17</td>
<td>2</td>
<td>8.5</td>
<td>55--72%</td>
</tr>
<tr>
<td>Rees et al, 1997\textsuperscript{29}</td>
<td>216</td>
<td>Poor performance</td>
<td>17</td>
<td>2</td>
<td>6</td>
<td>No difference between treatment arms</td>
</tr>
<tr>
<td>Plataniotis et al, 2002\textsuperscript{30}</td>
<td>92</td>
<td>Poor performance</td>
<td>22.5</td>
<td>5</td>
<td>6</td>
<td>76%</td>
</tr>
<tr>
<td>Bezjak et al, 2003\textsuperscript{31}</td>
<td>230</td>
<td>Mostly locally advanced</td>
<td>10</td>
<td>1</td>
<td>4.2</td>
<td>39%</td>
</tr>
<tr>
<td>Sundstrom et al, 2004\textsuperscript{32}</td>
<td>421</td>
<td>Stage III, IV/Mostly KPS 70--80</td>
<td>17</td>
<td>2</td>
<td>8.2</td>
<td>Better symptom control and QOL in 20-Gy arm</td>
</tr>
<tr>
<td>Kramer et al, 2005\textsuperscript{33}</td>
<td>297</td>
<td>Stage IIA, IIIB, IV/Mostly ECOG 3--4</td>
<td>16</td>
<td>2</td>
<td>10.9% at 1 y</td>
<td>30 Gy in 10 fractions/Better 22 wk posttreatment</td>
</tr>
<tr>
<td>Senkus-Konefka et al, 2005\textsuperscript{34}</td>
<td>100</td>
<td>Inoperable/Median ECOG of 2</td>
<td>30</td>
<td>10</td>
<td>19.6% at 1 y</td>
<td>P = .03</td>
</tr>
</tbody>
</table>

Gy indicates grays; MRC, Medical Research Council; WHO, World Health Organization performance status score; QOL, quality of life; KPS, Karnofsky performance status score; ECOG, Eastern Cooperative Oncology Group performance status score.
Superior Sulcus Tumor
Superior sulcus tumors

- Preoperative RT f/b extended surgical resection: most common treatment.
- Radiotherapy: a primary treatment, for inoperable superior sulcus tumors
- Palliation of pain in up to 90 percent of the patients.
- Doses of 20 to 80 Gy have been used
- A dose of at least 60 Gy is recommended for primary radiotherapy.
Small Cell Lung Cancer

- Limited disease: confined to the hemithorax.
- Extensive: extends beyond the hemithorax.
- Most of the improvement in outcome was attributed to more effective combination chemotherapy regimens.
- Locoregional therapy alone, either surgery or RT, improved the short-term survival only slightly.
• Role of RT proven once distant metastasis was controlled & local failure was apparent.
Small Cell Lung Cancer

• Thoracic RT and Prophylactic Cranial Irradiation.
• TRT concurrent with chemotherapy.
• Early TRT showed better outcome than late.
• Accelerated hyperfractionation better than daily fractions (5yr survival 28% vs 21%)
• No significant difference in local tumor control or survival with treatment between 45 Gy and 65 Gy when effective chemotherapy was given.
Prophylactic Cranial Irradiation

- Brain metastases - 10% at presentation
  - 80% at 2 yrs*
- Irradiation of entire intracranial contents
- Lower border at C2-3 vertebra
- Doses 24 – 30 Gy @ 3 Gy/#
- Increased the 3 year survival from 18% to 26%#

Thank you