SBRT for Advanced Stage Lung Cancer — Can It Work?

Rachel A. Hackett  CMD, RT(T)
LUNG CANCER

- Remains leading cause of cancer death
  - 224,200 new cases anticipated in 2014
  - 159,260 deaths
- Approximately 75% NSCLC
  - 15-20% diagnosed with localized disease
    - Surgery is mainstay of treatment
      - 5-yr survival rates of 65-70%
  - 80-85% present with either
    - Mediastinal or supraclavicular lymph node spread (N2 disease, Stage III)
    - Metastases (Stage IV)
• Even with excellent performance status and minimal N2 or metastatic disease
  • Often NOT candidates for curative surgery
  • Treated with chemotherapy and/or RT

• Overall survival remains dismal
Current standards of care

3D CRT:
- HyperFx RT
- HypoFx RT

1970s to Date: Virtually all combinations of radiation, chemotherapy and surgery have been attempted.
NSCLC: STAGES III and IV

- Addition of chemotherapy associated with OS improvement
  - Statistically significant
    - But < 10% improvement
  
- Comes at the expense of a large increase in Grade 3 Toxicities
Survival Results for Stage III NSCLC (9410)

**Concurrent vs. Sequential Chemo-RT**

<table>
<thead>
<tr>
<th></th>
<th>Dead/Total</th>
<th>MST</th>
</tr>
</thead>
<tbody>
<tr>
<td>STD 50</td>
<td>163/199</td>
<td>14.6 mo.</td>
</tr>
<tr>
<td>STD 1</td>
<td>147/200</td>
<td>17.1 mo.</td>
</tr>
</tbody>
</table>

*P-value (log-rank): 0.038*

*This is state of the art?*
## RTOG 94-10

<table>
<thead>
<tr>
<th>Arm</th>
<th>#</th>
<th>Chemo</th>
<th>RT</th>
<th>Gr3 Acute/Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seq</td>
<td>203</td>
<td>CP/Vbl</td>
<td>60</td>
<td>30%/14%</td>
</tr>
<tr>
<td>Con QD</td>
<td>204</td>
<td>CP/Vbl</td>
<td>60</td>
<td>48%/15%</td>
</tr>
<tr>
<td>Con BID</td>
<td>204</td>
<td>CP/VP16</td>
<td>69.6</td>
<td>62%/16%</td>
</tr>
</tbody>
</table>

This is state of the art? Plus, it's quite toxic!
Sequential ChemoRT vs RT Alone
Le Chevalier et al, JNCI 1991

<table>
<thead>
<tr>
<th></th>
<th>RT</th>
<th>CT/RT</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr LC</td>
<td>17%</td>
<td>15%</td>
<td>NS</td>
</tr>
<tr>
<td>2 yr OS</td>
<td>14%</td>
<td>21%</td>
<td>0.08</td>
</tr>
<tr>
<td>3 yr OS</td>
<td>4%</td>
<td>12%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Metastasis rate significantly lower with chemo/RT ($p<0.001$)
At 5 years, local control 8%

This is state of the art?
Plus, it’s quite toxic!
+ terrible local control!
3D CRT TOXICITY

- Late pulmonary
- Esophagitis
- Granulocytopenia
- Neutropenic Infection
- Nausea/ Vomiting
NSCLC: STAGES III and IV

- 2012 RTOG 9410 results:
  - Modern SOC = concurrent chemotherapy and radiation
    - 5 yr OS of 16%

What we are doing is not working.
SBRT demonstrates local control rates exceeding 90%.

- Uses very tight margins with IGRT to precisely deliver high doses (10 Gy to 34 Gy) of RT in 1 to 5 treatments over 1-14 days maximum
  - (Compared with 1.8 Gy to 2.5 Gy) over 30 or more treatments without IGRT.

- SBRT is now the standard of care for medically inoperable, early stage NSCLC patients.
3D vs SBRT

Five Year Overall Survival With Radiation

Conventional Radiation Therapy

SBRT
LYMPH NODES

Wait, with SBRT???
EARLY STAGE NSCLC LNs

Radiotherapy field size

Gross tumor only

Gross tumor + prophylactic
• 25-35% Rate of nodal mets
• Regional nodal failure rate in 3D CRT appears to be 5-15%
  • Even when these nodes are not intentional targets
• Suggested explanation that the incidental RT dose to high-risk nodal volumes may be significant enough to sterilize microscopic disease
  • Kepka et al. noted a decline in rate of nodal recurrences as incidental doses increased beyond a threshold of approx. 15 Gy.
• If incidental doses of 15 Gy delivered over 30 or more fractions can diminish nodal recurrence, then doses seen in our study (delivered over just 3 Fx) may certainly be sufficient to have a similar effect.
An adaptation of the IASLC Lymph Node Map

Supraclavicular Zone
- Low cervical
- Supraclavicular
- Sternal notch sides

Superior Mediastinal Nodes
Upper Zone
- R. Upper paratracheal
- L. Upper paratracheal
- Prevascular
- Retrotracheal
- R. Lower paratracheal
- L. Lower paratracheal

Inferior Mediastinal Nodes
Subcarinal Zone
- Subcarinal
- Paraesophageal (below carina)
- Pulmonary Ligament

N1 Nodes
Hilar/Interlobar Zone
- Hilar
- Interlobar

Peripheral Zone
- Lobar
- Segmental
- Subsegmental

Aortic Nodes
- Subaortic
- Para-aortic (ascending aorta or phrenic)
INCIDENTAL LN DOSE

- SBRT demonstrates local control rates exceeding 90%
  - Treatment of choice for medically inoperable, early stage NSCLC
- Recent study (Grills, et al. 2010)
  - Reduced regional nodal recurrence after SBRT to peripheral Stage I NSCLC compared with surgery
    - As of 2011, the incidental dose delivered to at-risk LNs during SBRT had not yet been described (as they had been for 3D CRT).
INCIDENTAL LN DOSE

• RPCI analyzed 38 consecutive early stage NSCLC patients treated with SBRT
  • 60 Gy in 3 Fx
  • Following RTOG 0236 constraints
    • Minimum of 9 non-coplanar 6-MV photons used
    • Avoided entrance through contralateral lung
    • Rx IDL ranged between 75% and 85%
    • Dose exceeding Rx dose was not allowed outside of PTV
INCIDENTAL LN DOSE

- Bilateral nodal stations retrospectively contoured
  - Level 2 (UPT)
  - Level 4 (LPT)
  - Level 10 (Hilar)
- Levels 2, 4, 10 studied
  - Frequent sites of postoperative regional failure
  - Frequent sites of failure after RT
  - Allowed easy extrapolation of dose to LN stations between 4 and 10
INCIDENTAL LN DOSE

- DVHs generated from original, unaltered treatment plan
- Patients categorized by tumor location
  - RUL: 14
  - LUL: 12
  - RLL: 6
  - LLL: 6
- All patients had T1-2N0 disease
- Tumor sizes ranged from 1.0 - 4.1 cm
INCIDENTAL LN DOSE
INCIDENTAL LN DOSE

SBRT to RLL Tumors

Volume of Defined Area (%) vs. Dose (Gy)

- Lt UPT
- Rt UPT
- Lt LPT
- Rt LPT
- Lt Hilar
- Rt Hilar
INCIDENTAL LN DOSE

SBRT to LLL Tumors

Volume of Defined Area (%) vs. Dose (Gy)

- Lt UPT
- Rt UPT
- Lt LPT
- Rt LPT
- Lt Hilar
- Rt Hilar
INCIDENTAL LN DOSE

Maximum and mean doses to lymph node stations by location

<table>
<thead>
<tr>
<th>Region of Tumor/Lymph Node Station</th>
<th>Average Maximum Point Dose, Gy (Range)</th>
<th>Average Mean Volume Dose, Gy (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RUL/2R</td>
<td>12.7 (0.6–40.8)</td>
<td>6.3 (0.4–22.8)</td>
</tr>
<tr>
<td>RUL/4R</td>
<td>17.3 (0.8–35.7)</td>
<td>7.8 (0.4–18.4)</td>
</tr>
<tr>
<td>RLL/10R</td>
<td>59.5 (21.1–100.5)</td>
<td>21.5 (9.3–45.4)</td>
</tr>
<tr>
<td>LUL/2L</td>
<td>11.7 (0.4–27.7)</td>
<td>5.2 (0.3–13.5)</td>
</tr>
<tr>
<td>LUL/4L</td>
<td>14.2 (6.6–22.7)</td>
<td>5.9 (1.1–10.9)</td>
</tr>
<tr>
<td>LLL/10L</td>
<td>69.1 (38.2–98.7)</td>
<td>15.6 (12.3–29.2)</td>
</tr>
</tbody>
</table>

- Average mean dose range 5.2 – 21.5 Gy
- Average max dose range 11.7 – 69.1 Gy
• It may be safe to treat single-fraction, low dose to hilar nodes, given experience with incidental dose during SBRT treatment of lower lobe tumors.
• Such dose to the most proximal hilar lymph nodes may be therapeutic.
• Current SOC (6 weeks of fractionated concurrent chemorad.) produces high toxicity and low efficacy.
• SBRT more effective for early stage disease
  • Let’s investigate SBRT for our advanced stage patients
• One Fx SBRT allows for quicker treatment and thus avoid toxicities with concurrent chemotherapy – full dose can be delivered later.
2005: Zielinski et al. described TEMLA as a novel approach to surgical staging of the mediastinum

TEMLA: Transcervical Extended Mediastinal Lymph Adenectomy
- 5-8cm collar incision in the neck
- Elevation of the sternal manubrium – special retractor
- Bilateral visualization of the laryngeal recurrent and vagus nerves
- Dissection of all mediastinal nodal stations except for station 9 (pulmonary ligament nodes)

VAMLA: Video-Assisted Mediastinal Lymphadenectomy
- Uses a video-assisted technique in lieu of special retractor
• 2011: Dr. Zielinski reported at the World Conference on Lung Cancer for surgical staging of LNs
  • Compared TEMLA with endoscopic staging with EBUS/ EUS

<table>
<thead>
<tr>
<th></th>
<th>TEMLA</th>
<th>EBUS/ EUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>98.6%</td>
<td>88.9%</td>
</tr>
<tr>
<td>Specificity</td>
<td>100%</td>
<td>98.7%</td>
</tr>
<tr>
<td>Negative predictive value (NPV)</td>
<td>99.7%</td>
<td>84.1%</td>
</tr>
<tr>
<td>Positive predictive value (PPV)</td>
<td>100%</td>
<td>99.1%</td>
</tr>
</tbody>
</table>

• Such impressive NPV and PPV has led to many in the thoracic surgery field to declare TEMLA the new gold standard for mediastinal staging.
A pilot study of SBRT after TEMLA for Stages III and IV NSCLC

• Primary Objective
  • Assess the feasibility/ toxicity of combining TEMLA with or without minimally invasive surgery and SBRT
  • Primary efficacy endpoint: portion of patients with ≥ Grade 3 toxicity anytime post-baseline visit until the final visit.

• Design
  • Stage III/ IV NSCLC
  • Central or peripheral tumor locations
  • ALL patients will receive TEMLA to remove med LNs
  • Followed by single fraction SBRT
    • 10 Gy to TEMLA bed
    • 30 Gy to primary tumor (if not surgically removed)
  • Chemotherapy may follow at discretion of Medical Oncologist
A pilot study of SBRT after TEMLA for Stages III and IV NSCLC

Eligible

Stage III
or
Solitary Mets
-Brain
-Bone
-Adrenal

Stratify by location of primary tumor

Peripheral
Central

Treatment

TEMLA

SBRT
30 Gy in 1 fraction to primary tumor + 10 Gy to positive nodal bed concurrently

Chemotherapy
At the discretion of med onc after 2 weeks
• Chemo regimens not prescribed – to be given at the discretion of the Medical Oncologist
• Patient will be eligible if primary tumor is removed without open thoracotomy
• 10 Gy SBRT will be delivered to any region of positive mediastinal nodes or positive margins
  • If mediastinal LNs are negative, they will not be treated.
10 Gy in 1 Fx to LN bed
30 Gy in 1 Fx to primary site, if not surgically removed
Respiratory motion accounted for (breath-hold preferred)
6MV x-ray photons
  > 6MV to 23 MV may be used in ≤ 2 beams that must travel more than a cumulative distance of 10 cm or more through soft tissue (NOT lung) to reach the isocenter
Heterogeneity correction ON
VMAT preferred
  IMRT and 3D CRT may be used if necessary
FFF beams
### Structure of Protocol

<table>
<thead>
<tr>
<th>PTV Volume (cc)</th>
<th>Ratio of Prescription Isodose Volume to the PTV Volume</th>
<th>Ratio of 50% Prescription Isodose Volume to the PTV Volume, $R_{50%}$</th>
<th>Maximum Dose (in % of dose prescribed) @ 2 cm from PTV in Any Direction, $D_{2cm}$ (%)</th>
<th>Percent of Lung Receiving 20 Gy Total or More, $V_{20}$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deviation</td>
<td>Deviation</td>
<td>Deviation</td>
<td>Deviation</td>
</tr>
<tr>
<td></td>
<td>None  Minor</td>
<td>None  Minor</td>
<td>None  Minor</td>
<td>None  Minor</td>
</tr>
<tr>
<td>1.8</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;5.9$  $&lt;7.5$</td>
<td>$&lt;50.0$  $&lt;57.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>3.8</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;5.5$  $&lt;6.5$</td>
<td>$&lt;50.0$  $&lt;57.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>7.4</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;5.1$  $&lt;6.0$</td>
<td>$&lt;50.0$  $&lt;58.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>13.2</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;4.7$  $&lt;5.8$</td>
<td>$&lt;50.0$  $&lt;58.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>22.0</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;4.5$  $&lt;5.5$</td>
<td>$&lt;54.0$  $&lt;63.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>34.0</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;4.3$  $&lt;5.3$</td>
<td>$&lt;58.0$  $&lt;68.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>50.0</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;4.0$  $&lt;5.0$</td>
<td>$&lt;62.0$  $&lt;77.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>70.0</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;3.5$  $&lt;4.8$</td>
<td>$&lt;66.0$  $&lt;86.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>95.0</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;3.3$  $&lt;4.4$</td>
<td>$&lt;70.0$  $&lt;89.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>126.0</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;3.1$  $&lt;4.0$</td>
<td>$&lt;73.0$  $&lt;91.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
<tr>
<td>163.0</td>
<td>$&lt;1.2$  $&lt;1.5$</td>
<td>$&lt;2.9$  $&lt;3.7$</td>
<td>$&lt;77.0$  $&lt;94.0$</td>
<td>$&lt;10$  $&lt;15$</td>
</tr>
</tbody>
</table>

**Note 1:** For values of PTV dimension or volume not specified, linear interpolation between table entries is required.

**Note 2:** Protocol deviations greater than listed here as "minor" will be classified as "major" for protocol compliance (see Section 6.7).
<table>
<thead>
<tr>
<th>Serial Tissue</th>
<th>Volume</th>
<th>Volume Max (Gy)</th>
<th>Max Point Dose (Gy)</th>
<th>Endpoint (≥Grade 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal Cord</td>
<td>&lt;0.35 cc</td>
<td>10 Gy</td>
<td>14 Gy</td>
<td>myelitis</td>
</tr>
<tr>
<td></td>
<td>&lt;1.2 cc</td>
<td>7 Gy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophagus*</td>
<td>&lt;5 cc</td>
<td>11.9 Gy</td>
<td>15.4 Gy</td>
<td>stenosis/fistula</td>
</tr>
<tr>
<td>Brachial Plexus</td>
<td>&lt;3 cc</td>
<td>14 Gy</td>
<td>17.5 Gy</td>
<td>neuropathy</td>
</tr>
<tr>
<td>Heart/Pericardium</td>
<td>&lt;15 cc</td>
<td>16 Gy</td>
<td>22 Gy</td>
<td>pericarditis</td>
</tr>
<tr>
<td>Great vessels</td>
<td>&lt;10 cc</td>
<td>31 Gy</td>
<td>37 Gy</td>
<td>aneurysm</td>
</tr>
<tr>
<td>Trachea and Large Bronchus*</td>
<td>&lt;4 cc</td>
<td>10.5 Gy</td>
<td>20.2 Gy</td>
<td>stenosis/fistula</td>
</tr>
<tr>
<td>Rib**</td>
<td>&lt;1 cc</td>
<td>22 Gy</td>
<td>30 Gy</td>
<td>Pain or fracture</td>
</tr>
<tr>
<td>Skin</td>
<td>&lt;10 cc</td>
<td>23 Gy</td>
<td>26 Gy</td>
<td>ulceration</td>
</tr>
<tr>
<td>Stomach</td>
<td>&lt;10 cc</td>
<td>11.2 Gy</td>
<td>12.4 Gy</td>
<td>ulceration/fistula</td>
</tr>
<tr>
<td>Parallel Tissue</td>
<td>Critical Volume (cc)</td>
<td>Critical Volume Dose Max (Gy)</td>
<td>Endpoint (≥Grade 3)</td>
<td></td>
</tr>
<tr>
<td>Lung (Right &amp; Left)</td>
<td>1500 cc</td>
<td>7 Gy</td>
<td>Basic Lung Function</td>
<td></td>
</tr>
<tr>
<td>Lung (Right &amp; Left)</td>
<td>1000 cc</td>
<td>7.4 Gy</td>
<td>Pneumonitis</td>
<td></td>
</tr>
</tbody>
</table>

* Avoid circumferential irradiation

** Rib limit may be exceeded if rib structure lies with PTV
STRUCTURE OF PROTOCOL

- Normal tissue contouring guidelines provided within protocol (same as RTOG 0915)
- IGRT daily
  - CBCT pre tx
  - CBCT during tx, as needed
  - Fluoroscopy of primary tumor
  - kV match orthogs
  - Portal image of selected beams
2 TARGETS
2 TARGETS
### SBRT LUNG DVH ANALYSIS

**MED S/P TEMLA**

**Radiation Oncologist:** J. Gomez  
**RPCI Case #:** 201-H223912

<table>
<thead>
<tr>
<th>Rx Dose (Gy)</th>
<th>30</th>
<th>Fractions:</th>
<th>1</th>
<th>Rx IDL (%)</th>
<th>79.17</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV vol (cc)</td>
<td>52.38</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 % Rx Dose</td>
<td>30 % Rx Dose</td>
<td>125 % Rx Dose outside PTV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 Gy vol (cc)</td>
<td>66.8552</td>
<td>16 Gy vol (cc)</td>
<td>226.076</td>
<td>31.6 Gy vol (cc)</td>
<td>2.80051</td>
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</tbody>
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### Prescription Dose Constraints

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Limit</th>
<th>Actual</th>
<th>Protocol Limit Met?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rx isodose Coverage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rx isodose (%)</td>
<td>≤ 90%</td>
<td>79.17</td>
<td>YES</td>
</tr>
<tr>
<td>% PTV covered</td>
<td>30 Gy</td>
<td>95</td>
<td>95.016</td>
</tr>
<tr>
<td>% PTV covered</td>
<td>27 Gy</td>
<td>95</td>
<td>99.991</td>
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</tbody>
</table>

### High Dose Spillage

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Limit</th>
<th>Actual</th>
<th>Protocol Limit Met?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vol outside PTV ≤ 100 % Rx dose (%)</td>
<td>≤ 5%</td>
<td>4.63</td>
<td>YES</td>
</tr>
<tr>
<td>Conformity Vol vs EL / Vol PTV</td>
<td>1.7</td>
<td>1.66</td>
<td>YES</td>
</tr>
</tbody>
</table>

### Low Dose Spillage

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Limit</th>
<th>Actual</th>
<th>Protocol Limit Met?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vol outside PTV ≤ 100 % Rx dose (%)</td>
<td>≤ 5%</td>
<td>4.92</td>
<td>YES</td>
</tr>
</tbody>
</table>

### Critical Structure Dose Constraints

<table>
<thead>
<tr>
<th>Organ</th>
<th>Parameter</th>
<th>Limit (Gy)</th>
<th>Actual (Gy)</th>
<th>Protocol Limit Met?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal Cord</td>
<td>Max Point Dose</td>
<td>14.0</td>
<td>13.1</td>
<td>YES</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Max Point Dose</td>
<td>15.4</td>
<td>13.5</td>
<td>YES</td>
</tr>
<tr>
<td>Bronchial</td>
<td>Max Point Dose</td>
<td>17.5</td>
<td>16.6</td>
<td>YES</td>
</tr>
<tr>
<td>Heart</td>
<td>Max Point Dose</td>
<td>22.0</td>
<td>21.1</td>
<td>NO</td>
</tr>
<tr>
<td>Great Vessels</td>
<td>Max Point Dose</td>
<td>31.0</td>
<td>24.6</td>
<td>YES</td>
</tr>
<tr>
<td>Trachea</td>
<td>Max Point Dose</td>
<td>20.2</td>
<td>12.1</td>
<td>YES</td>
</tr>
<tr>
<td>Large Branches</td>
<td>Max Point Dose</td>
<td>20.2</td>
<td>16.3</td>
<td>NO</td>
</tr>
<tr>
<td>Lung (Right)</td>
<td>Max Point Dose</td>
<td>20.2</td>
<td>16.3</td>
<td>NO</td>
</tr>
</tbody>
</table>

| Lung (Left) | Max Point Dose | 23.0 | 7.2 | YES |

### Additional Notes:

- MIN DEV = 23.3
- MIN DEV ALLOWED = 4.92
1 TARGET: LN BED
1 TARGET: LN BED
1 TARGET: LN BED
1 TARGET: LN BED
### SBRT LUNG DVH ANALYSIS

**Parameter** | **Limit** | **Actual** | **Protocol Limit Met?**
--- | --- | --- | ---
Rx Isodose Coverage
Rx Isodose (%) | > 60%, < 50% | 90% | YES
% PTV covered by 10 Gy | 95 | 96.2706 | YES
% PTV covered by 9 Gy | 99 | 99.9976 | YES

**High Dose Spillage**
Vol outside PTV x 100% Rx dose (cc) ≤ 15% PTV volume | 7.83 | 0.028 | YES
Conformally - Vol rx DL / Vol PTV | 1.2 | 1.01 | YES

**Low Dose Spillage**
Max dose @ 2 cm (Gy) | 6.20 | 4.912 | YES
Vol 90% Rx Dose / Vol PTV | 5.95 | 3.48 | YES

**Organ** | **Parameter** | **Limit (Gy)** | **Actual (Gy)** | **Protocol Limit Met?**
--- | --- | --- | --- | ---
Spinal Cord | Max Point Dose | 14.0 | 2.2 | YES
<0.36 cm receives | 10.0 | 1.9 | YES
<1.2 cm receives | 7.0 | 1.5 | YES
Eosophagus | Max Point Dose | 15.4 | 6.9 | YES
<5.0 cm receives | 11.9 | 3.6 | YES
Branchial Plexus | Max Point Dose | 17.5 | 0.2 | YES
<3.0 cm receives | 14.0 | 0.1 | YES
Heart | Max Point Dose | 22.0 | 3.1 | YES
<15.0 cm receives | 16.0 | 0.6 | YES
Great Vessels | Max Point Dose | 37.0 | 11.1 | YES
<10.0 cm receives | 31.0 | 10.2 | YES
Thorax | Max Point Dose | 20.2 | 11.1 | YES
<4.0 cm receives | 10.5 | 2.2 | YES
Large Bronchus | Max Point Dose | 20.2 | 11.1 | YES
<4.0 cm receives | 10.5 | 9.0 | YES
Skin | Max Point Dose | 26.0 | 2.3 | YES
<10.0 cm receives | 23.0 | 1.6 | YES
LUNGS | <1000.0 cm receives | 7.0 | 0.4 | YES
<3000.0 cm receives | 7.4 | 1.5 | YES
<table>
<thead>
<tr>
<th>PROCESS</th>
<th>BREATH-HOLDS</th>
<th>TIME TO DELIVER</th>
<th>MDs ROLE (IN MINUTES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBCT</td>
<td>5 in 63”</td>
<td>4’30”</td>
<td>5’22”</td>
</tr>
<tr>
<td>358° ARC 1</td>
<td>6 in 65”</td>
<td>4’20”</td>
<td></td>
</tr>
<tr>
<td>1260 MUs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>358° ARC 2</td>
<td>6 in 63”</td>
<td>7’</td>
<td></td>
</tr>
<tr>
<td>1260 MUs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>358° ARC 3</td>
<td>5 in 61”</td>
<td>6’40”</td>
<td></td>
</tr>
<tr>
<td>1260 MUs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Tx TIME w/ BREATH-HOLD
2 TARGETS: 30 Gy + 10 Gy

- Original plan was 7 full arcs
- BH tx time not prohibitive
- Used 10 arc segments
  - 9 @ 36°
  - 1 @ 34°
- From time of setup to off the table: 1hr, 15mins

- Also acquired kV matches and an ANT fluoro field
  - 2'40"

<table>
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<th>MDs ROLE (IN MINUTES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBCT 1</td>
<td>3 in 52”</td>
<td>6'00”</td>
<td>15’20”</td>
</tr>
<tr>
<td>CBCT 2</td>
<td>9 in 1’44”</td>
<td>11’50”</td>
<td>5’6”</td>
</tr>
<tr>
<td>Segment 1</td>
<td>2 in 18”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Segment 2</td>
<td>1 in 17”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Segment 3</td>
<td>1 in 19.7”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Segment 4</td>
<td>2 in 21”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Segment 5</td>
<td>1 in 16.6”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Segment 6</td>
<td>4 in 23”</td>
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<tr>
<td>Segment 7</td>
<td>3 in 20”</td>
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<td>Segment 8</td>
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<td>Segment 9</td>
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</tr>
<tr>
<td>Segment 10</td>
<td>2 in 18.4”</td>
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</tr>
</tbody>
</table>
IN SUMMARY

- Current SOC Stage III/IV NSCLC
  - Quite toxic
  - 6 weeks to deliver
  - Extended period of time for recovery
  - Inadequate local control
  - Constrains the doses of systemic therapy

- Pilot study
  - Establish feasibility of combining novel therapies of SBRT and TEMLA, followed by targeted chemotherapy
• If proven feasible
• And proven again in a subsequent, larger study
• Then this approach will
  • Improve local control
  • Diminish toxicity
  • Improve overall survival
  • By allowing more aggressive systemic therapy
THANK YOU

Anurag K. Singh  MD
Simon D. Fung-Kee-Fung  MD
Jorge A. Gomez  MD
REFERENCES


CENTRALLY LOCATED TUMORS

• Definition of central tumor location: Tumor location within the zone of the proximal bronchial tree + 2cm in all directions

• Toxicity reported from the initial University of Indiana study
  • 2-year freedom from severe toxicity
    • 83% of peripheral lung tumors
    • 54% of central lung tumors
  • Upon further follow-up, this difference lost statistical significance (p= 0.088).
  • However, the fear of central irradiation had already become established and RTOG 0813 was launched.