ARROCase

Early-stage NSCLC: SBRT/SABR

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Case: Clinical Presentation

• 60yo white female
• 50pk-yr former smoker with COPD had CXR showing suspicious right lung nodule
• CT showed spiculated RLL mass 1.7 x 1.5 x 1.5cm
• Lesion avid on PET without any other areas suspicious for disease
Work-Up: Imaging

CT

PET
Work-Up: Pathology

- CT-guided biopsy showed: Invasive moderately differentiated squamous cell carcinoma

1. www.pathologyoutlines.com/topic/lungtumorSCC.html
Work-Up: Operative Candidate?

• Guideline Criteria for Surgical Consideration\(^1,2\)
  – Pneumonectomy: FEV1 > 80% and > 2L
  – Lobectomy: FEV1 > 70% and > 1.5L
  – Wedge: FEV1 > 0.6L
  – If FEV1 or DLCO < 80%, calculate predicted post-op lung function (PPO)
    • FEV1<40% PPO or DLCO<40% PPO: Increased Risk
    • SAO2 < 90% or FEV1 < 30%: Increased risk
    • Patient unable to walk 1 flight of stairs: Increased Risk

• Patient FEV1 = 38%, DLCO = 46%, exercise intolerant; Deemed Medically Inoperable

Epidemiology

• In the US, NSCLC is the second most common non-skin cancer
  – Incidence behind prostate in men and breast in women

• In US, Lung cancer is leading cause of cancer death (more than breast, prostate, and colorectal combined)

Risk Factors

• 80-90% of cases associated with smoking
  – Incidence peaked around 1990 in men; 20 years later in women; related to smoking adoption and cessation
• Radon exposure is 2nd most common in US
• Additional risk factors: asbestos, arsenic, hydrocarbon exposure

Tumor Staging, AJCC 7th Edition

- **T0**: No evidence of primary tumor
- **Tis**: Carcinoma in situ
- **T1**: 3cm or less without invasion of main bronchus
  - **T1a**: Tumor ≤ 2cm
  - **T1b**: 2cm < Tumor ≤ 3cm
- **T2**: 3cm < Tumor ≤ 7cm, or involving main bronchus 2cm or more distal to carina, or invading visceral pleura, or associated with atelectasis or obstructive pneumonitis
  - **T2a**: 3cm < Tumor ≤ 5cm
  - **T2b**: 5cm < Tumor ≤ 7cm
- **T3**: Tumor < 7cm or invading: parietal pleura, chest wall, diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium, or main bronchus within 2cm of carina, or separate tumor nodules in the same lobe
- **T4**: Tumor invading mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; or separate tumor in different ipsilateral lobe
## Group Staging, AJCC 7th Edition

<table>
<thead>
<tr>
<th>T-Stage</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
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<td>IA</td>
<td>IIA</td>
<td>IIIA</td>
<td>IIIB</td>
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<tr>
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<td>T4</td>
<td>IIIA</td>
<td>IIIA</td>
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</table>
Anatomy: Central vs. Peripheral

- Per RTOG 0236 Protocol Definition, Peripheral: Not within 2cm of proximal bronchial tree (lobar bronchi)

Diagnosis/Work-Up

• NCCN workup for all NSCLC:
  – Path review, H&P, CT chest and upper abdomen including adrenals, CBC, Chemistry, Smoking Cessation

• Stage IA
  – PFTs
  – Bronchoscopy
  – Pathologic mediastinal LN evaluation (category 2B)
  – PET/CT

1. NCCN Guidelines. v7.2015.
NCCN Treatment Guidelines

• Proven T1a/b N0
  – Operable: surgical exploration and resection with mediastinal LN dissection or sampling
  – Medically Inoperable: Definitive RT including SABR
    • Dose (NCCN v7.2015): Goal BED≥100Gy
      – 25-34Gy / 1 fx: small <2cm peripheral tumors >1cm from CW
      – 45-60Gy / 3 fx: peripheral tumors and >1cm from CW
      – 48-50Gy / 4 fx: central or peripheral <4-5cm, esp <1cm CW
      – 50-55Gy / 5 fx: central or peripheral tumors, esp <1cm CW
      – 60-70Gy / 8-10fx: central tumors (>5fx is not SABR billable)

1. NCCN Guidelines. v7.2015.
Treatment

• Patient treated with SABR (stereotactic ablative radiation therapy, AKA SBRT)
• 5,400 cGy over 3 fractions of 1,800 cGy per fraction via with non-coplanar arc-based 6MV photon beams

1. NCCN Guidelines. v7.2015.
Treatment Planning - Simulation

- Supine
- Arms above head
  - May have arms at side for robotic linac non-arc based treatment
- Vac-lock bag
- 4D-CT simulation used to assess internal tumor motion
Treatment Planning

• Motion management options with 4D-CT sim
  – If little tumor motion (<1cm)
    • Free breathing during treatment designed to cover entire track of tumor motion (using ITV)
  – If tumor motion irregular or large (>1cm):
    • Breath Hold (deep inspiration preferred)
    • Respiratory Gating: Free breathing with treatment only delivered at specific period of breath cycle
    • May consider abdominal compression to minimize motion

Target Volumes

• Image fusion with PET performed; MIP also overlaid for target delineation

• GTV: Gross tumor as visible CT and PET
• ITV: Gross tumor taking account motion on 4D-CT using MIP (maximum intensity projection)
• PTV: ITV with 0.5cm expansion

Target Volumes

- GTV/ITV (Red)
- PTV (Cyan)
Prognostic / Predictive Models

• Dose with $\text{BED}_{10} \geq 100^{1-105^2}\text{Gy}$ associated with significantly improved Local Control and survival

  – 54Gy in 3 fractions: $\text{BED}_{10} = 126\text{Gy}$

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Cumulative Dose Volume Histogram

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<tr>
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<tbody>
<tr>
<td>SPINAL CORD</td>
<td>Approved</td>
<td>100.0 / 100.0</td>
<td>18.3 cm³</td>
<td>3.9 cGy</td>
<td>739.5 cGy</td>
<td>177.0 cGy</td>
<td>12.3 cGy</td>
<td>53.6 cGy</td>
<td>212.1 cGy</td>
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<td>ESOPHAGUS</td>
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<td>100.0 / 100.0</td>
<td>19.2 cm³</td>
<td>8.6 cGy</td>
<td>1116.0 cGy</td>
<td>196.2 cGy</td>
<td>11.5 cGy</td>
<td>31.8 cGy</td>
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<td>TRACHEA &amp; BRONCHI</td>
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<td>100.0 / 100.0</td>
<td>30.7 cm³</td>
<td>1.9 cGy</td>
<td>1155.6 cGy</td>
<td>215.4 cGy</td>
<td>14.0 cGy</td>
<td>36.6 cGy</td>
<td>294.6 cGy</td>
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<td>PRV CORD</td>
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<td>100.0 / 99.9</td>
<td>44.2 cm³</td>
<td>9.1 cGy</td>
<td>1175.3 cGy</td>
<td>185.3 cGy</td>
<td>12.6 cGy</td>
<td>51.1 cGy</td>
<td>237.3 cGy</td>
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<td>AORTA</td>
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<td>73.5 cm³</td>
<td>12.3 cGy</td>
<td>1192.9 cGy</td>
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<td>CHESTWALL</td>
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<td>100.0 / 100.0</td>
<td>110.9 cm³</td>
<td>18.0 cGy</td>
<td>2953.3 cGy</td>
<td>795.7 cGy</td>
<td>23.4 cGy</td>
<td>221.9 cGy</td>
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<tr>
<td>LUNG TOTAL - PTV</td>
<td>Approved</td>
<td>100.0 / 100.0</td>
<td>4440.7 cm³</td>
<td>0.8 cGy</td>
<td>5835.1 cGy</td>
<td>216.7 cGy</td>
<td>10.6 cGy</td>
<td>39.3 cGy</td>
<td>508.9 cGy</td>
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<td>LUNG RIGHT</td>
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<td>100.0 / 100.0</td>
<td>2503.0 cm³</td>
<td>0.9 cGy</td>
<td>6179.4 cGy</td>
<td>334.6 cGy</td>
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<td>54.9 cGy</td>
<td>732.6 cGy</td>
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<tr>
<td>LUNG LEFT</td>
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<td>1850.2 cm³</td>
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<td>ITV</td>
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Dose Coverage / Heterogeneity

- Prescribed such that 95% of PTV covered by 100% isodose
- Goal: 110% > Dmax > 140% of prescription
- R50 (ratio of 50% isodose volume to PTV volume) < 3-6 based on PTV size (larger should have smaller R50)
OAR / Plan Evaluation

- Protocol Goal R50 values in RTOG 0236:

<table>
<thead>
<tr>
<th>Maximum PTV Dimension (cm)</th>
<th>Ratio of Prescription Isodose Volume to the PTV Deviation</th>
<th>Ratio of 50% Prescription Isodose Volume to the PTV, R_{50}% Deviation</th>
<th>Maximum Dose 2 cm from PTV in any Direction, D_{2\text{cm}} (Gy) Deviation</th>
<th>Percent of Lung receiving 20 Gy total or more, V_{20} (%) Deviation</th>
<th>PTV Volume (cc)</th>
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<td>2.0</td>
<td>&lt;1.2</td>
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<td>&lt;3.9-4.1</td>
<td>28.1-30.1</td>
<td>10-15</td>
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<tr>
<td>2.5</td>
<td>&lt;1.2</td>
<td>1.2-1.4</td>
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<td>28.1-30.1</td>
<td>10-15</td>
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<tr>
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<td>1.2-1.4</td>
<td>&lt;3.9-4.1</td>
<td>28.1-30.1</td>
<td>10-15</td>
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<tr>
<td>3.5</td>
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<td>&lt;2.9</td>
<td>44.3-46.3</td>
<td>10-15</td>
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</tbody>
</table>

OAR Dose Constraints

- OAR constraints (3 fractions)\(^1,^2\)
  - Spinal Cord 18Gy max
  - Esophagus 25.2-27Gy max, <5cc 17.1Gy
  - Trachea 30Gy max
  - Bronchi 23.1-30 Gy max, <5cc 18.9Gy
  - Rib 30-37 Gy max, <30cc 30Gy
  - Brachial Plexus 24 Gy max
  - Chest Wall\(^3,^4\): V30 < 30-50cc

1. NCCN Guidelines. v7.2015.
Daily Setup

• Daily cone-beam CT used for localization
  – Alternatively can use fiducial implants correlated with bony anatomy if volumetric imaging not available
Data Supporting Treatment

• Early data from Indiana U\textsuperscript{1}, and Japan\textsuperscript{2}
• “Control” depends on area of interest\textsuperscript{2-5}
  – Tumor control > 90%
  – Local-Regional control may be closer to 60% in medically inoperable patients, especially those not undergoing surgical LN staging prior to SBRT
• Survival for Medically Inoperable with SBRT
  – 2-3yr OS\textsuperscript{2-6}: \approx 40-71%

Relevant Data

• RTOG 0236\textsuperscript{1}
  – Phase II, 55 inoperable pt, peripheral T1-T2N0 NSCLC <5cm
  – SBRT 54Gy/3fx
  – 3-yr Outcomes
    • Tumor Control (in-field): 98%
    • Local Control (in-lobe): 91%
    • Locoregional Control: 87%
    • 22% DM, median OS 48mo

RTOG 0236: 2014 ASTRO Abstract

• Median follow-up 4.0yr (7.2yr for survivors)

5-year Outcomes:
  – Primary Tumor Failure Rate: 7%
  – Primary tumor & involved lobe (Local) failure: 20%
  – Local-Regional (Includes Node) Failure: 38%
  – Disseminated Failure: 31%
  – DFS: 26%
  – OS: 40%

Toxicity Data

• Phase II IU 2006 data\(^1\) showed Grade 3-5 toxicity 17% in peripheral vs 46% in central tumors
  – 2009 update\(^2\) showed observed Grade 3+ toxicity peripheral 10% vs central 27% (p=.09)
    • Central location reclassified according to RTOG 0236

• Note: Dose recommendations are modified and more variable for central tumors compared to this peripheral case

References

1. www.pathologyoutlines.com/topic/lungtumorSCC.html