Challenging Cases in Lung SBRT

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Challenging Cases in Lung SBRT

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  Washington University School of Medicine

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  Clinician Scientist, Ontario Institute for Cancer Research

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  University of Manchester & The Christie NHS Foundation Trust

Moderator:
- David Palma, MD, PhD, FRCPC
  Professor, Western University
  Clinician Scientist, Ontario Institute for Cancer Research
Publications

Coming Soon in the JTO:

**Stereotactic Radiation for Lung Cancer: A Practical Approach to Challenging Scenarios**
Neal Andruska, MD, PhD; Hayley B. Stowe, MD; Cathryn Crockett, MBBCH, BAO, MRCP, FRCR; Wei Liu, MD; David Palma, MD; Corinne Faivre-Finn, FRCR, MD, PhD; Shahed N. Badiyan, MD

Additional publications:

A Primer on Interstitial Lung Disease and Thoracic Radiation

Brief Report on Radiological Changes following Stereotactic Ablative Radiotherapy (SABR) for Early-Stage Lung Tumors: A Pictorial Essay

Stereotactic Body Radiation Therapy for Central Early-Stage NSCLC: Results of a Prospective Phase I/II Trial

Radiosensitivity of Lung Metastases by Primary Histology and Implications for Stereotactic Body Radiation Therapy Using the Genomically Adjusted Radiation Dose

Biologically Effective Dose in Stereotactic Body Radiotherapy and Survival for Patients with Early-Stage NSCLC
Disclosures

› **Corinne Faivre-Finn, FRCR MD PhD** discloses she receives research funding from Astra Zeneca, MSD Pharmaceuticals and Elekta and is on an advisory board and scientific committees for Astra Zeneca.

› **David Palma, MD, PhD, FRCPC** has no relevant financial relationships to disclose.

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All relevant financial relationships have been mitigated.
Ultra-central Early Stage Non-Small Cell Lung Cancer

Shahed N. Badiyan, MD
Assistant Professor
Washington University
Polling Question 1

Which of the following is the most common source of high grade toxicity in patients treated with hypofractionated radiation/SBRT for ultra-central early stage non-small cell lung cancer?

A. Chest wall toxicity
B. Spinal cord myelitis
C. Pulmonary hemorrhage
D. Pericarditis
Case Presentation

• 78 year old male underwent annual chest CT for surveillance of a left lung nodule found years earlier after a motor vehicle collision.

• Medical History:
  • 30 pack-year smoking history. Quit 30 years ago.
    • FEV1 = 98% predicted (3.9 L)
    • DLCO = 74% predicted

• Chest CT: New 2.8 cm mass in superior RLL. Stable LLL nodule.
Workup

CT Chest:
- Right lower lobe azygo-esophageal recess mass, 2.8 cm, abutting right main stem bronchus
- No lymphadenopathy

PET/CT Scan:
- Right lower lobe azygo-esophageal recess hypermetabolic lesion, SUVmax 21.4
- No FDG avid lymphadenopathy
- No distant metastases
Tissue Diagnosis and Staging

- **Flexible Bronchoscopy:**
  - No endobronchial tumor seen

- **EBUS for mediastinal staging:**
  - No visibly enlarged nodes
  - EBUS transbronchial FNA of RLL mass:
  - Pathology: poorly differentiated NSCLC, favor squamous cell carcinoma
Case: Our Patient’s Treatment

• What would you recommend?

• Offered RLL superior segmentectomy by thoracic surgeon
• Repeat bronchoscopy in OR by surgeon found extrinsic compression of right mainstem bronchus without frank invasion.
• Surgery aborted due to likelihood of needing pneumonectomy or complex reconstruction of airway

• Patient referred for SBRT
Common Dose Options

• Central:
  • 50-55 Gy in 5 Fx (common in the U.S.)
  • 60 Gy in 8 Fx (common in Canada / Europe)
  • 48 Gy in 4 Fx
  • 60 Gy in 5 Fx (MTD as per RTOG 0813)

• Ultracentral:
  • 60 Gy in 8 Fx
  • 50 Gy in 5 Fx
  • 60 Gy in 12 Fx
  • 60 Gy in 15 Fx
  • Conventional RT
RTOG 0813

Safety and Efficacy of a Five-Fraction Stereotactic Body Radiotherapy Schedule for Centrally Located Non–Small-Cell Lung Cancer: NRG Oncology/RTOG 0813 Trial

Andrea Bezjak, MD1; Rebecca Paulus2; Laurie E. Gaspar, MD2; Robert D. Timmerman, MD3; William L. Straube, MS3; William F. Ryan, MD2; Yolanda I. Garces, MD2; Anthony T. Pu, MD2; Anurag K. Singh, MD2; Gregory M. Videtic, MD2; Ronald C. McGarry, MD, PhD1; Purvesh Iyengar, MD, PhD1; Jason R. Pantarotto, MD1; James J. Urbanic, MD1; Alexander Y. Sun, MD1; Megan E. Daly, MD1; Inga S. Grills, MD1; Paul Spenduto, MD1; Daniel P. Normolle, PhD1; Jeffrey D. Bradley, MD1; and Hak Choy, MD1

**TABLE A2. Dose Limits Indices as Specified in the Protocol: Organs at Risk**

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Volume (mL)</th>
<th>Volume Max, Gy (Gy/fx)</th>
<th>Max Point Dose, Gy (Gy/fx)</th>
<th>Avoidance End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spinal cord</td>
<td>&lt; 0.25</td>
<td>22.5 (4.5)</td>
<td>30 (6)</td>
<td>Myelitis</td>
</tr>
<tr>
<td></td>
<td>&lt; 0.5</td>
<td>13.5 (2.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral brachial plexus</td>
<td>&lt; 3</td>
<td>30 (6)</td>
<td>32 (6.4)</td>
<td>Neuropathy</td>
</tr>
<tr>
<td>Skin</td>
<td>&lt; 10</td>
<td>30 (6)</td>
<td>32 (6.4)</td>
<td>Ulceration</td>
</tr>
<tr>
<td>Parallel*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung (right and left side)</td>
<td>1,500</td>
<td>12.5 (2.5)</td>
<td></td>
<td>Basic lung function</td>
</tr>
<tr>
<td>Lung (right and left side)</td>
<td>1,000</td>
<td>13.5 (2.7)</td>
<td></td>
<td>Pneumonitis</td>
</tr>
<tr>
<td>Serial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophagus, nonadjacent wall</td>
<td>&lt; 5</td>
<td>27.5 (5.5)</td>
<td>105†</td>
<td>Stenosis/fistula</td>
</tr>
<tr>
<td>Heart/pericardium</td>
<td>&lt; 15</td>
<td>32 (6.4)</td>
<td>105†</td>
<td>Pericarditis</td>
</tr>
<tr>
<td>Great vessels, nonadjacent wall</td>
<td>&lt; 10</td>
<td>47 (9.4)</td>
<td>105†</td>
<td>Aneurysm</td>
</tr>
<tr>
<td>Trachea and ipsilateral bronchus, nonadjacent wall</td>
<td>&lt; 4</td>
<td>18 (3.6)</td>
<td>105†</td>
<td>Stenosis/fistula</td>
</tr>
</tbody>
</table>

Abbreviations: fx, fraction; Max, maximum.
*Listed are critical volume and critical volume dose maximum.
†Percentage of planning target volume (PTV) prescription.
# Ultra-central Definitions and Outcomes

<table>
<thead>
<tr>
<th>Study</th>
<th>Definition of Ultra-central</th>
<th>Dose/Fractionation</th>
<th>2-yr Local Control</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>HILUS Phase II, 2021 (n=65)</td>
<td>≤ 1 cm from PBT</td>
<td>56 Gy/8 fx (100%) 150% hotspot</td>
<td>83%</td>
<td>Grade 3+: 34% Grade 5: 15%</td>
</tr>
<tr>
<td>Breen, 2021 (n=110)</td>
<td>GTV abutting PBT, trachea; PTV overlap PBT, trachea; GTV ≤ 1 cm from PBT</td>
<td>50 Gy/5 fx (57%) 60 Gy/8 fx (15%) 48 Gy/4 fx (13%)</td>
<td>84%</td>
<td>Grade 5 (4%)</td>
</tr>
<tr>
<td>RTOG 0813, 2019 (n=120)</td>
<td>≤ 2 cm from PBT</td>
<td>50-60 Gy/5 fx</td>
<td>87.9-89.4%</td>
<td>7.2% DLTs</td>
</tr>
<tr>
<td>Raman, 2018 (n=26)</td>
<td>PTV overlapping PBT, trachea, esophagus, pulmonary vein/artery</td>
<td>60 Gy/8 fx (77%) 50 Gy/10 fx (12%)</td>
<td>100%</td>
<td>Grade 2-3: 7.9% Grade 4-5: 0%</td>
</tr>
<tr>
<td>Tekatli, 2016 (n=47)</td>
<td>PTV overlapping trachea or main bronchi</td>
<td>60 Gy/12 fx 140% hotspot</td>
<td>78%</td>
<td>Grade 3+: 38% Grade 5: 13%</td>
</tr>
<tr>
<td>Li, 2014 (n=82)</td>
<td>Dose constraints for 50 Gy in 4 fx not met</td>
<td>70 Gy/10 fx (100%)</td>
<td>96.2%</td>
<td>Grade 3: 3.6% Grade 5: 1.2%</td>
</tr>
</tbody>
</table>

Systematic Review

Safety and Effectiveness of Stereotactic Ablative Radiotherapy for Ultra-Central Lung Lesions: A Systematic Review

- High doses to PBT
- Endobronchial disease
- Bevacizumab or anticoagulants
Current Trial: SUNSET

- Multicenter phase I dose-finding study

- Starting dose: 60 Gy in 8 fx. Hot spot limited to 120%

- Ultracentral definition: PTV touches or overlaps the central bronchial tree, esophagus, pulmonary vein, or pulmonary artery

Giuliani et al, Clin lung cancer 2018
Patients with ultra-central NSCLC
T1-3 (≤6 cm) N0 M0

<table>
<thead>
<tr>
<th>DOSE LEVELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>Dose per fraction:</td>
</tr>
<tr>
<td>Number of fractions:</td>
</tr>
<tr>
<td>Total Dose</td>
</tr>
</tbody>
</table>

Giuliani et al, Clin lung cancer 2018
Patient Plan

60 Gy in 12 fx

VMAT 2 arcs:
20-181 degrees Clockwise & Counter clockwise

Hot spot of 35%
### Dose Constraints

#### Table 2  Recommended Dose Constraints

<table>
<thead>
<tr>
<th>Organ</th>
<th>Metric</th>
<th>Fraction</th>
<th>5/6</th>
<th>8/10</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal canal</td>
<td>Max</td>
<td></td>
<td>30 Gy</td>
<td>32 Gy</td>
<td>39.5 Gy</td>
</tr>
<tr>
<td>Spinal canal PRV (3 mm)</td>
<td>Max</td>
<td></td>
<td>32 Gy</td>
<td>34 Gy</td>
<td>42 Gy</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Max</td>
<td></td>
<td>40 Gy</td>
<td>45 Gy</td>
<td>50.5 Gy</td>
</tr>
<tr>
<td>5 cc</td>
<td></td>
<td></td>
<td>35 Gy</td>
<td>40 Gy</td>
<td>48 Gy</td>
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<tr>
<td>Brachial plexus</td>
<td>Max</td>
<td></td>
<td>32 Gy</td>
<td>39 Gy</td>
<td>50 Gy</td>
</tr>
<tr>
<td>Heart</td>
<td>Max</td>
<td></td>
<td>62 Gy</td>
<td>64 Gy</td>
<td>66 Gy</td>
</tr>
<tr>
<td>10 cc</td>
<td></td>
<td></td>
<td>50 Gy</td>
<td>60 Gy</td>
<td>62 Gy</td>
</tr>
<tr>
<td>Trachea</td>
<td>Max</td>
<td></td>
<td>62 Gy</td>
<td>64 Gy</td>
<td>66 Gy</td>
</tr>
<tr>
<td>10 cc</td>
<td></td>
<td></td>
<td>50 Gy</td>
<td>60 Gy</td>
<td>62 Gy</td>
</tr>
<tr>
<td>Proximal bronchus</td>
<td>Max</td>
<td></td>
<td>62 Gy</td>
<td>64 Gy</td>
<td>66 Gy</td>
</tr>
<tr>
<td>10 cc</td>
<td></td>
<td></td>
<td>50 Gy</td>
<td>60 Gy</td>
<td>62 Gy</td>
</tr>
<tr>
<td>Non-GTV lung</td>
<td>Mean</td>
<td></td>
<td>&lt;12 Gy</td>
<td>&lt;12 Gy</td>
<td>&lt;14 Gy</td>
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<td>10 cc</td>
<td></td>
<td></td>
<td>50 Gy</td>
<td>60 Gy</td>
<td>62 Gy</td>
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<tr>
<td>Aorta and major vessels</td>
<td>Max</td>
<td></td>
<td>62 Gy</td>
<td>64 Gy</td>
<td>64 Gy</td>
</tr>
<tr>
<td>10 cc</td>
<td></td>
<td></td>
<td>50 Gy</td>
<td>60 Gy</td>
<td>60 Gy</td>
</tr>
<tr>
<td>Stomach and intestines</td>
<td>Max</td>
<td></td>
<td>40 Gy</td>
<td>45 Gy</td>
<td>50 Gy</td>
</tr>
<tr>
<td>10 cc</td>
<td></td>
<td></td>
<td>35 Gy</td>
<td>40 Gy</td>
<td>48 Gy</td>
</tr>
</tbody>
</table>

#### 12 Fraction Regimen Dose Constraints

<table>
<thead>
<tr>
<th>Organ</th>
<th>Volumetric Constraint</th>
<th>Max point dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal cord</td>
<td>D0.35cc &lt; 31.2 Gy</td>
<td>37.8 Gy</td>
</tr>
<tr>
<td>Esophagus</td>
<td>D5cc &lt; 21.6 Gy</td>
<td>48 Gy</td>
</tr>
<tr>
<td>Trachea &amp; Bronchi</td>
<td>D5cc &lt; 52 Gy</td>
<td>59 Gy</td>
</tr>
<tr>
<td>Great Vessels</td>
<td>D10cc &lt; 55.7 Gy</td>
<td>62.9 Gy</td>
</tr>
<tr>
<td>Heart</td>
<td>D15cc &lt; 38.2 Gy</td>
<td>43.7 Gy</td>
</tr>
</tbody>
</table>

Abbreviations: GTV = gross tumor volume; PRV = planning organ-at-risk volume.
Patient Plan

- **Trachea/Bronchi**
- **Great Vessels**
- **PTV**
- **ITV**
3 month post-treatment CT
Key Points

- Ultra-central tumors require more caution
- Use dose constraints for great vessels, trachea/large bronchi
- Beware of high doses to the PBT, endobronchial invasion, and bevacizumab or anticoagulation
- Optimal doses and constraints will hopefully be determined soon!
Resources

Management of Multiple Lung Lesions

David Palma, MD, PhD, FRCPC
Professor, Western University
Clinician Scientist, Ontario Institute for Cancer Research
Case Presentation

• 85 year-old man with prior history of a T3N2c squamous cell carcinoma of the supraglottis treated with chemoradiation in 2010.

• Presented in May 2017 with a cough. CXR showed nodules in right lung and CT scan ordered.

• Three lesions, all new from 2010.
Case Presentation

• Medical History: Diabetes, angina, moderate COPD (80 pack years) – FEV1 = 55% predicted.

• Repeat CT 3 months later shows growth of all 3.

• PET-CT shows all three lesions have SUVmax between 6-9
Polling Question 2

In patients with multiple lung cancers detected on initial scan, with no prior scans, the lesions are most likely to be:

A. Synchronous primaries
B. One primary with two metastases
C. Two primaries with metastasis from one of them
D. Impossible to know
Polling Question 3

What would you recommend for this patient?

A. Observation
B. Resection of all lesions
C. Systemic therapy
D. SABR to all sites
Clinical Considerations

• Do we need a biopsy? If so, how many lesions do we biopsy?

• Are these multiple primaries or mets?

• Observation or Treatment? Which options?
One Primary or Multiple

The IASLC Lung Cancer Staging Project: Background Data and Proposed Criteria to Distinguish Separate Primary Lung Cancers from Metastatic Foci in Patients with Two Lung Tumors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer

“It is easier to determine that two tumors are different than that they are the same; finding similarities does not establish that they are the same.”

Genomic profiles analyzed from 15 lung adenocarcinomas in 6 patients

- All suggested independent primary tumors (not metastases)


Plan Evaluation: One Additional Parameter

**Application of Critical Volume-Dose Constraints for Stereotactic Body Radiation Therapy in NRG Radiation Therapy Trials**

Timothy A. Ritter, PhD,*,†,‖ Martha Matuszak, PhD,*,†,‖ Indrin J. Chetty, PhD,*,†,‖ Charles S. Mayo, PhD,*,†,‖ Jackie Wu, PhD,*,†,‖ Puneeth Iyengar, MD, PhD,*,†,‖ Michael Weldon, MS,*,†,‖ Clifford Robinson, MD,*,†,‖ Ying Xiao, PhD,*,†,‖ and Robert D. Timmerman, MD,*,†,‖

CV12.5 = volume receiving 12.5 Gy or less

5 fraction constraint:
1.5 L receiving <12.5 Gy

Our Case: 60 Gy in 8 fractions
Each PTV optimized separately. There was some contribution across plans, so each PTV was optimized to be under-covered; good coverage on composite plan.

Goal: 1500 cc with a critical volume threshold of 14.3 Gy (8 fractions)
Key Points

• Synchronous lesions are most likely to be synchronous primaries (polling question #1)

• The best treatment is unknown and the approach should be individualized. Both surgery and SABR have advantages and disadvantages.
Re-SBRT of Lung Cancer

Shahed N. Badiyan, MD
Assistant Professor
Washington University
Polling Question 4

Grade 3+ toxicity rates with re-SBRT for lung cancer are approximately:

A. 10%
B. 30%
C. 60%
D. 80%
Case Presentation

- 73 year old male underwent annual chest CT for surveillance for surveillance of pulmonary nodules 3 years prior

- Medical History:
  - 40 pack-year smoking history. Continues to smoke 5 cig/day
  - Colon cancer, T3N1M0, 4 years prior, s/p hemicolecction and FOLFOX x 6 cycles
  - Type II DM on insulin
  - COPD

- Chest CT: New 9 mm LUL spiculated nodule. No lymphadenopathy
Workup

CT Chest:
- LUL 9 mm spiculated nodule
- No lymphadenopathy

PET/CT Scan:
- LUL nodule SUV max 1.7. Other nodules not FDG avid.
- No FDG avid lymphadenopathy
- No distant metastases

- EBUS:
  - No visibly enlarged nodes
  - EBUS transbronchial FNA of LUL nodule
  - Pathology: moderately differentiated adenocarcinoma, TTF-1 +, likely lung primary
Case: First Treatment

- Patient referred for SBRT
- Received 54 Gy in 3 fx every other day
  - 7 field FFF plan
Case: Patient Follow-up

- Did well for 2.5 years

- CT chest showed growth of LUL nodule (now 13 mm) inferior to radiation fibrosis.

- PET/CT: LUL nodule inferior to radiation fibrosis has SUVmax of 4.2
Case: Metachronous NSCLC in prior SBRT field

- Recommendation at Multi-D Tumor Board:
  - No biopsy due to location
  - Not a good surgical candidate
  - Recommend SBRT
# Re-SBRT Definitions and Outcomes

<table>
<thead>
<tr>
<th>Study</th>
<th>Definition of Re-SBRT</th>
<th>Dose for re-SBRT</th>
<th>Local control outcomes</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kennedy et al. 2020 (n=21)</td>
<td>Within 1 cm of PTV or overlap of ≥ 25% isodose lines</td>
<td>50 Gy/5 fx (57%)</td>
<td>2-yr 81%</td>
<td>Gr 2 pneumonitis: 10% Gr 2 chest wall: 19% Gr 3+: 0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>54 Gy/3 fx (43%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hearn et al. 2014 (n=10)</td>
<td>Marginal failures within 1 cm of PTV</td>
<td>50 Gy/ 5 fx (70%)</td>
<td>60%</td>
<td>Gr 1-2 fatigue: 30% Gr 1-2 chest wall: 50% Gr 3+: 0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60 Gy/ 3 fx (30%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peulen et al. 2011 (n=29)</td>
<td>&gt;50% overlap of PTVs</td>
<td>30 Gy / 2 fx (34%)</td>
<td>5 mo 52%</td>
<td>Gr 3-4: 28% Gr 5 hemorrhage: 10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40 Gy/ 5 fx (28%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>45 Gy/ 3 fx (21%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Kennedy WR, et al. Radioth Oncol 2020
Peulen H, et al. Radioth Oncol 2011
Re-SBRT Meta-analysis

- Re-SBRT for 625 lung lesions in 595 patients
- 86% primary lung cancer
- 51% First course RT conventional fx
- 45% central recurrence
- 2-year LC 73%
- 2-year OS 54%
- Grade 3+ toxicity: 9.8%
- Grade 5: 1.5%

Viani et al Am J Clin Oncol 2020
Re-SBRT Meta-analysis

- LC associated with:
  - Re-SBRT dose ($p=0.034$)
  - Tumor size ($p=0.04$)

- Cumulative dose $>145$ Gy2:
  - 15% risk of Grade 3+ toxicity

- Cumulative dose $<145$ Gy2
  - 3% risk of Grade 3+ toxicity

Viani et al Am J Clin Oncol 2020
Suggested Treatment Algorithm

Isolated Local Recurrence → Multidisciplinary Evaluation

Operable

Lobectomy with nodal dissection (preferred)

Or

Sublobar resection +/- nodal dissection/sampling

Kennedy WR, et al. Radioth Oncol 2020
Case: Second Treatment

- Received 50 Gy in 5 fx delivered once daily
- VMAT 2 arcs: 175 to 345 degrees clockwise and counter clockwise
- Max dose 63.7 Gy located in GTV
- PBT max 37 Gy
- Pulmonary artery max 59 Gy
- Esophagus max 8 Gy
- Heart max 7 Gy
Case: Cumulative Radiation Plan

- Cumulative Max 117 Gy in lung parenchyma
- PBT max 50 Gy
  - No overlap on PBT
- Pulmonary artery max 70 Gy
- Esophagus max 11 Gy
- Heart max 14 Gy
- Cord max 9 Gy
Case: Patient Follow-up

- Now 3.5 years out from second course of SBRT
- Post-radiation fibrosis in LUL
- Asymptomatic
- No evidence of recurrent colon cancer or lung cancer
Future Directions

• Ideal fractionation scheme

• Development of validated dose constraints

• Utility of advanced technologies
  • Proton Therapy
  • MRI-guided SBRT

• Role of systemic therapies with SBRT
Key Points

› Multidisciplinary discussion crucial

› Tumor size and cumulative dose associated with toxicity
  › Local control associated with total dose

› Risk rises with cumulative EQD2 > 145 Gy
  › Create cumulative plan to evaluate dose to OARs

› Balance the benefit of treatment with risk of toxicity
  › Grade 3+ toxicity rate approx. 10%

Kennedy WR, et al. Repeat stereotactic body radiation therapy (SBRT) for salvage of isolated local recurrence after definitive lung SBRT. Radiother and Oncol. 2020;142,230-235

Hearn JWD, et al. Salvage Stereotactic Body Radiation Therapy (SBRT) for Local Failure After Primary Lung SBRT. In J Radiat Oncol Biol Phys 2014;90(2)402-406.

Peulen H, et al. Toxicity after reirradiation of pulmonary tumours with stereotactic body radiotherapy. Radiother Oncol 2011;101(2)260-266

Early-Stage NSCLC with ILD

David Palma, MD, PhD, FRCPC
Professor, Western University
Clinician Scientist, Ontario Institute for Cancer Research
Case Presentation

- 67 year old woman presents with a new, growing nodule in the right lower lobe.

- She has a history of idiopathic pulmonary fibrosis diagnosed five years prior, and is dyspneic with any activity but not yet on oxygen. Prednisone-dependent at 15 mg daily.

- Med Hx: also CAD, MR, PVD with bypass, DM II, HTN, pulmonary hypertension
Investigations

- The nodule was detected incidentally on CT chest 6 months ago, measuring 3.2 cm in size, growing to 3.5 cm in size on repeat scan 3 months ago
PET/CT: SUVmax 3.2
Investigations

• CT-guided lung biopsy shows adenocarcinoma.

• PFTs: FEV1=101% predicted; DLCO/VA: 55%

• Brain imaging negative
Physical Exam

- Looks her staged age, not dyspneic at rest, but dyspneic getting to the exam table

- No lymphadenopathy palpable

- Bibasilar crackles on auscultation

- No other pertinent findings
Polling Question 5

Which treatment option would you recommend?

A. Surgical resection
B. SABR
C. Thermal ablation
D. Systemic therapy
E. Observation
Treatment

- PFTs were acceptable for resection but in the context of other co-morbidities, surgeon advised non-operative management

- Consented to treatment with SABR, aware of potential increased risk of pulmonary toxicity due to ILD

- Treatment given as 60 Gy in 8 fractions
Follow-up

• Followed by Resp, Rad Onc, Vascular, Nephrology

• 0-3 months post-treatment:
  • No change in respiratory status
  • Fatigue

• 3 Month CT:
  • Lesion now 2.1 cm, surrounding post-radiation change
  • New nodules in RML measuring 6 and 8 mm
  • Right hilar fullness
3 month scans
Follow-up

- 4-months post-treatment: febrile, chest pain, SOB
  - Treated with clarithromycin, improved back to baseline

- 9 months post-treatment
  - Exacerbation of ILD requiring admission, levofloxacin, prednisone 50 mg daily
  - Initiation of oxygen: remained oxygen dependent for life
CT: 1 yr post-treatment
Subsequent follow-up

- Recurrent pneumonias and ILD exacerbations, interfering with ADLs
- Progressive intrathoracic metastatic disease
- Not eligible for cytotoxic chemotherapy, EGFR-negative

- Symptom management by palliative care team
ILD is a large collection of lung diseases, also called diffuse parenchymal lung disease.
ILD Classification

A Primer on Interstitial Lung Disease and Thoracic Radiation

Christopher D. Goodman, MD • Suzan F.M. Nijman, MD • Suresh Senan, MRCP, FRCR, PhD • Esther J. Nossent, MD • Christopher J. Ryerson, MD, FRCPC • Inderdeep Dhaliwal, MD, FRCPC • X. Melody Qu, MD, FRCPC • Joanna Laba, MD, FRCPC • George B. Rodrigues, MD, PhD, FRCPC, FASTRO • David A. Palma, MD, PhD, FRCPC

on behalf of the International Association for the Study of Lung Cancer Advanced Radiation Technology Committee

Published: February 24, 2020 • DOI: https://doi.org/10.1016/j.jtho.2020.02.005
Fibrotic ILDs

• Idiopathic pulmonary fibrosis (IPF)
  • Honeycombing!!

• Connective tissue disease related
  • e.g. lupus, scleroderma

• Hypersensitivity pneumonitis
  • bird-fancier’s lung

• Drug-induced

• Pneumoconioses
  • silica, asbestos

• Other/unclassified
CT Findings

- reticulation

- traction bronchiectasis

- patchy GGO
**Idiopathic Pulmonary Fibrosis**

IPF is a chronic, progressive fibrotic interstitial lung disease of unknown origin.

HRCT images: usual interstitial pneumonia (UIP) pattern

**UIP pattern, with extensive honeycombing:** basal predominant, peripheral predominant reticular abnormality, with multiple layers of honeycombing.

**Possible UIP pattern:** peripheral predominant, basal predominant reticular abnormality with moderate amount of ground glass abnormality, but without honeycombing.
ILD and SABR Systematic Review

Critical Review

Treatment-Related Toxicity in Patients With Early-Stage Non-Small Cell Lung Cancer and Coexisting Interstitial Lung Disease: A Systematic Review

Hanbo Chen, MD,* Suresh Senan, MRCP, FRCR, PhD,† Esther J. Nossent, MD,‡ R. Gabriel Boldt, RLIS,* Andrew Warner, MSc,* David A. Palma, MD, PhD, FRCPC,* and Alexander V. Louie, MD, PhD, FRCPC*

*Department of Radiation Oncology, London Health Sciences Centre, London, Ontario, Canada, and Departments of †Radiation Oncology and ‡Pulmonology, VU University Medical Center, Amsterdam, The Netherlands

<table>
<thead>
<tr>
<th>Group</th>
<th>Mortality</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ILD subtypes</td>
<td>15.6%</td>
<td>25%</td>
</tr>
<tr>
<td>IPF only studies</td>
<td>33%</td>
<td>71%</td>
</tr>
</tbody>
</table>

ILD and Surgery

Impact of interstitial lung disease on short-term and long-term survival of patients undergoing surgery for non-small-cell lung cancer: analysis of risk factors

Luca Voltolini, Stefano Bongiolatti, Luca Luzzi, Elena Bargagli, Antonella Fossi, Claudia Ghiribelli, Paola Rottoli and Giuseppe Gotti

Table 3: Procedure-specific mortality and incidence of ARDS/ALI after pulmonary resection

<table>
<thead>
<tr>
<th>Procedure</th>
<th>ILD group (n = 37)</th>
<th>Non-ILD group (n = 738)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean hospital stay</td>
<td>12.51 ± 5.5</td>
<td>9.58 ± 4.1</td>
<td>≤0.01</td>
</tr>
<tr>
<td>Total deaths</td>
<td>3 (8.1%)</td>
<td>10 (1.4%)</td>
<td>≤0.01</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>1/4 (25%)</td>
<td>3/90 (3.3%)</td>
<td></td>
</tr>
<tr>
<td>Lobectomy</td>
<td>2/30 (66%)</td>
<td>7/528 (1.3%)</td>
<td></td>
</tr>
<tr>
<td>Sublobar resection</td>
<td>0/3</td>
<td>0/114</td>
<td></td>
</tr>
<tr>
<td>ARDS/ALI</td>
<td>5 (13.5%)</td>
<td>17 (2.3%)</td>
<td>≤0.01</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>1/4 (25%)</td>
<td>7/90 (7.8%)</td>
<td></td>
</tr>
<tr>
<td>Lobectomy</td>
<td>3/30 (10%)</td>
<td>8/528 (1.5%)</td>
<td></td>
</tr>
<tr>
<td>Sublobar resection</td>
<td>1/3 (33%)</td>
<td>2/114 (1.8%)</td>
<td></td>
</tr>
</tbody>
</table>

ILD: interstitial lung disease; ARDS: acute respiratory distress syndrome; ALI: acute lung injury.

Fibrotic Interstitial Lung Disease and NSCLC T1-2N0M0

Stratify by ILD Severity using ILD-GAP Index

Cohort I
ILD-GAP Index: ≤2

Cohort II
ILD-GAP Index: 3-5

Cohort III
ILD-GAP Index: ≥6

SABR 50 Gy in 5 fractions with pre-specified de-escalation rules based on Cohort and ILD subtype

Follow-up for survival and toxicity

The ILD-GAP Model

Chest 2014; 145(4):723-28

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILD subtype</td>
<td>0</td>
</tr>
<tr>
<td>IPF</td>
<td>0</td>
</tr>
<tr>
<td>Unclassifiable ILD</td>
<td>0</td>
</tr>
<tr>
<td>CT-ILD/idiopathic NSIP</td>
<td>-2</td>
</tr>
<tr>
<td>Chronic HP</td>
<td>-2</td>
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<tr>
<td>Gender</td>
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</tr>
<tr>
<td>Female</td>
<td>0</td>
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<tr>
<td>Male</td>
<td>1</td>
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<tr>
<td>Age, yr</td>
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</tr>
<tr>
<td>≤ 60</td>
<td>0</td>
</tr>
<tr>
<td>61-85</td>
<td>1</td>
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<tr>
<td>&gt; 85</td>
<td>2</td>
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<tr>
<td>Physiology</td>
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<tr>
<td>FVC, % predicted</td>
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<tr>
<td>&gt; 75%</td>
<td>0</td>
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<tr>
<td>50-75%</td>
<td>1</td>
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<tr>
<td>&lt;50%</td>
<td>2</td>
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<tr>
<td>DLCO, % predicted</td>
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<tr>
<td>&gt; 50%</td>
<td>0</td>
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<tr>
<td>36-65%</td>
<td>0</td>
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<tr>
<td>≤ 35%</td>
<td>2</td>
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<tr>
<td>Cannot perform</td>
<td>3</td>
</tr>
</tbody>
</table>

Total possible points 8

ILD and SABR

› Many consider ILD and IPF a relative contraindication to SABR, but alternative options may be limited

› In this scenario, multidisciplinary opinion is required, with careful discussion with the patient

› Options:
  › SABR: as gentle a dose as possible
  › Observe (if life expectancy short)
  › Systemic therapies
Take Home Messages

• The management of lung cancer in the setting of ILD is challenging

• Surgical resection preferred if adequate pulmonary reserve

• If not surgery, then approach will depend on patient & tumor board consideration of relative risks of treatment vs. untreated lung cancer