Radiation Therapy for Lung Cancer

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Disclosures

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Overview: Current use of radiation for Lung Cancer

• Current Status of SBRT for early stage NSCLC
  – Role in operable patients
  – Next directions

• Current Status of Radiation for Locally Advanced NSCLC
  – Next directions

• Lung cancer palliation with radiation

• Management of radiation-induced lung toxicity
Radiation for Lung Cancer

- Early stage medically inoperable disease
- Early stage medically operable (investigational)
- Locally advanced (IIIA/IIIB)
- Small Cell Lung Cancer
- Palliation of metastatic disease
- Ablative therapy for oligometastatic/oligoprogressive disease
Radiotherapy for Lung Cancer: Key Issues

• Minimizing Toxicity
  – Small margins (daily setup is crucial)
  – Accounting for lung motion in the planning process
  – Ability to sculpt dose around critical structures

• Maximizing Tumor Control
  – Ability to deliver ablative doses while sparing normal tissues
Treatment Planning Challenges

• Proximity to critical structures
• Irregularly shaped target volumes
• Moving tumors
Lung SBRT: Overview and Uses

- Use of highly conformal radiation using ablative doses over 1-5 treatments
Lung Stereotactic Body Radiotherapy (SBRT)

• Standard of care option for medically inoperable patients with early stage non-small cell lung cancer (NSCLC)
• Non-invasive, outpatient procedure over 3-5 sessions
• High local control rates (>90%)
Methods of compensating for respiratory motion

- Free Breathing ITV
- Abdominal Compression
- Respiratory Gating
- Tumor Tracking
Defining an ITV: 4DCT
Respiratory Gating
Abdominal Compression
Lung SBRT: Clinical Outcomes
RTOG 0236 (JAMA 2010)

- Phase II study; medically inoperable pts with T1-2 N0 NSCLC
- 54 Gy/3 fx
- 3 yr Primary tumor control 97.6%
- 3 yr Local Control 90.6%
- 3 year Distant Failure Rate:
  - T1: 14.7%
  - T2: 47%
- 3 yr Disease-Free Survival 48.3%
- 3 yr Overall Survival 55.8%
- 3.6% rate of grade 4 adverse events
Current Use of SBRT

- Standard Option for Medically Inoperable, peripheral early stage (T1-2 NSCLC < 5 cm)
  - 54 Gy in 3 fractions
- Investigational in medically operable patients
- Investigational for tumors >5cm
- Some concerns of increased toxicity for central lung tumors (within 2 cm of proximal bronchial tree), but protracted regimens of 4-8 fractions are generally considered safe
  - 48-50 Gy in 5 fractions
  - 50-60 Gy in 5 fractions
  - 60 Gy in 8 fractions
Sample SBRT Plan: T2aN0M0 Central NSCLC
Sample SBRT Plan: T1N0M0 Peripheral
SBRT for Operable Patients: Current Status

- Several studies have attempted to compare surgery and SBRT in a prospective, randomized fashion and failed to accrue.

- Many retrospective analyses on this topic, but selection bias remains a major problem.
  - Propensity matching attempts to limit the bias of retrospective studies by matching patients on baseline characteristics, and reduces influence of varying baseline characteristics.

- Surgical management remains the standard therapy for medically operable patients in absence of completed, randomized trials.
## Prospective Randomized Trials Evaluating SBRT for Operable Patients

<table>
<thead>
<tr>
<th>Trial</th>
<th>Eligibility</th>
<th>Design</th>
<th>Status</th>
</tr>
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<tbody>
<tr>
<td>STARS</td>
<td>T1-2aN0M0 &lt;4 cm, fit for lobectomy</td>
<td>Randomized Phase III comparing lobectomy to SBRT</td>
<td>Terminated due to poor accrual</td>
</tr>
<tr>
<td>ROSEL</td>
<td>T1-2aN0M0 &lt;4 cm fit to tolerable lobectomy</td>
<td>Randomized Phase III comparing lobectomy to SBRT</td>
<td>Terminated due to poor accrual</td>
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<tr>
<td>ACOSOG Z0499</td>
<td>Peripheral NSCLC ≤ 3 cm; “high” surgical risk</td>
<td>Randomized Phase III comparing sublobar resection to SBRT</td>
<td>Terminated due to poor accrual</td>
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<tr>
<td>JoLT-Ca STABLE-MATES</td>
<td>Peripheral NSCLC ≤ 4 cm; “high” surgical risk</td>
<td>Pre-randomization design; phase III</td>
<td>Actively accruing</td>
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<tr>
<td>Veterans Affairs Lung Cancer Surgery Or Stereotactic Radiotherapy Trial (VALOR)</td>
<td>T1-2N0M0&lt;5 cm fit for lobectomy</td>
<td>Randomized Phase III</td>
<td>Actively accruing</td>
</tr>
<tr>
<td>RTOG Foundation 3502 (POSTILV)</td>
<td>T1N0M0 ≤ 3 cm fit for lobectomy</td>
<td>Randomized Phase II</td>
<td>Actively accruing</td>
</tr>
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SBRT Patterns of Failure

- Primary (in-lobe) control: 75-98%
- Locoregional control: 60-85%
- Distant control: 55-80%
Next Directions in SBRT

• Strategies to reduce regional/distant failure
  – Adjuvant chemotherapy
  – Immunotherapy
  – Targeted therapy
Eligible Early Stage NSCLC patient (n=198) Randomize

UC Davis Stage I Trial

1 22 43 64 85 106

SBRT 10-12.5 Gy/fraction QOD x 5

Priming

Concurrent

Consolidation

Follow-up

Follow-up
(Chemo)Radiation for Locally Advanced NSCLC

- Definitive Concurrent Chemoradiation for Unresectable IIIA/IIIB disease

- Pre-operative CRT for well-selected, resectable IIIA disease with low-burden N2 disease
Defining Targets

- **Gross Tumor Volume (GTV)**: Radiographically involved tumor or nodes
- **Internal Target Volume (ITV)**: Encompasses tumor excursion due to respiratory motion
- **Clinical Target Volume (CTV)**: Includes additional margin for microscopic spread
- **Planning Target Volume (PTV)**: Additional margin for daily setup error
Locally Advanced NSLC – Technical Advances in RT Planning

- **Intensity Modulated Radiotherapy (IMRT) and Volume Modulated Arc Therapy (VMAT)**
  - Allow for concave and convex dose distributions
  - For appropriately selected patients improves sparing of normal tissues
  - Creates sharp dose gradients

- **4D CT simulation**
  - Allows accurate estimation of tumor motion with breathing
Lung Cancer Target Definition
IMRT T4N0M0 NSCLC
IMRT T4N0M0 NSCLC: Sagittal/Coronal
IMRT Planning: T2N3M0 adenocarcinoma
IMRT Planning: T2N3M0 adenocarcinoma
Daily Image Guidance: CBCT
Potential Side Effects of Thoracic Radiotherapy

- **Lungs**
  - Inflammation
  - Scarring
  - Decreased pulmonary function

- **Heart**
  - Pericarditis
  - Scarring/valve damage/increased risk of MI or cardiac death

- **Spinal Cord**
  - Myelopathy

- **Esophagus**
  - Esophagitis
  - Scarring

- Radiation-induced cancers
Reducing Toxicity for Locally Advanced Lung Cancer

- Pneumonitis
  - Major complication of RT for lung cancer
  - Recent pooled analysis suggests ~30% rate of symptomatic pneumonitis following CRT for stage III NSCLC (Palma et al, 2013)
  - Highest risk groups include elderly and those receiving concurrent carbo/taxol
Approaches to reducing pneumonitis risk

• Reduced margins for setup error and internal motion
  – Daily image guidance
  – Motion management (compression or gating)
  – RT to elective nodal regions is now infrequently used as isolated nodal failure is rare
Emerging Approaches to reducing pneumonitis risk

- Identification and selective avoidance of high-functioning lung sub-regions
  - 4D CT
  - SPECT
  - Other functional imaging techniques
4DCT Functional Lung Avoidance

4D CT image → Displacement vector field → Ventilation image

- Deformable image registration (DIR)
- Quantification of regional volume change

Slide courtesy of T. Yamamoto PhD, UC Davis
Treatment of Radiation Pneumonitis

• Long prednisone taper is standard for dyspnea
  – 5-6 weeks, starting at 20 mg TID with rapid fall off
Radiotherapy for metastatic lung cancer

• Palliation of painful bone metastases
  – 1-10 fractions

• Brain metastases
  – Gamma knife (≈1-4 lesions)
  – Whole brain radiation (≈30 Gy in 10 fractions)

• SBRT for oligometastatic disease in good performance status patients (investigational)
Conclusions

• Radiotherapy plays an important role in the management of lung cancer
  – SBRT is a standard option for early stage, medically inoperable disease
  – Concurrent or sequential chemoradiation for locally advanced disease
    • Studies are evaluating ways of reducing side effects for these patients
  – Palliation
    • Bone mets, brain mets, airway obstruction, SVC syndrome
Thank you!

Feel free to email me with additional questions  
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