Stereotactic Body Radiation Therapy and Radiofrequency Ablation

2014 Masters of Minimally Invasive Surgery

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Duke Cancer Institute
Case Presentation I: Patient ER

74 y/o male with A1A referred for lung transplantation

- On 4L O₂, FEV₁ = 17%
- CT chest demonstrates 2.9 cm proximal RLL nodule
- PET avid
- Declared medically unfit for lower lobectomy
- Referred for SBRT
Stereotactic Body Radiation Therapy

What is it?

- Very large doses of radiation per fraction
- Multiple beams (10-12)
- Unique radiobiological effects
- Specific regimens will vary
Stereotactic Body Radiation Therapy

**Necessary Components**

- Comfortable immobilization
- Compensation for respiratory motion
- Accurate set-up
- Effective and safe dose
  - Location
  - Size
## EBRT for Stage I NSCLC

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Dose (median)</th>
<th>Survival (5-year)</th>
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<tbody>
<tr>
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<tr>
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a) *IJROBP* 1993;27:507  
b) *IJROBP* 1995;31:261  
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e) *Radiotherapy and Oncology* 1997;42:31
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<tr>
<td>JCOG 0403 (Kyoto, Japan)</td>
<td>45</td>
<td>12 Gy X 4</td>
<td>Overall Survival</td>
<td>T1 97%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T2 83% (3)</td>
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<td>Ricardi (Torino, Italy)</td>
<td>62</td>
<td>15 Gy X 3 (80%)</td>
<td>OS (3) 57%</td>
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<td></td>
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<td>Baumann (Scandinavia)</td>
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<td>15 Gy X 3 (67%)</td>
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<td>Takeda (Tokyo, Japan)</td>
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<td>10 Gy X 5 (80%)</td>
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<td>T1 93% (3)</td>
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<td></td>
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Patterns of Failure: EBRT
Patterns of Failure: SBRT

Distant Metastases
Case Presentation: Patient ER

Referred for SBRT

- 58 Gy over 8 fractions (proximal location)
- F/U CT chest at 6 months shows residual scar...
Case Presentation: Patient ER

- ...but had new pleural nodularity, worrisome for metastatic disease.
Conventional EBRT

- Overall Survival: ~30%;40%
- Cause-Specific Survival

SBRT

- Overall Survival: ~60%;80%
- Cause-Specific Survival

Caveats
Improved staging
Supportive care

*estimated from data provided
Grade 3 or 4 toxicities in up to 25-35% reported

Chest wall toxicity (16% with rib fx’s and pain if peripheral tumors)

Brachial plexopathy for apical tumors (16% in one study)

Proximal lesions can be dangerous
  - 20% with severe toxicity, 9% mortality
  - Adjust dosing regimens
Follow-up Imaging

NCCN Guidelines Version 1.2013
Non-Small Cell Lung Cancer

No evidence of clinical/radiographic disease), stages I-IV:

- H&P and chest CT ± contrast every 6-12 mo for 2 y (category 2B), then H&P and a non-contrast-enhanced chest CT annually (category 2B)
- Smoking cessation advice, counseling, and pharmacotherapy
- PET or brain MRI is not indicated
Ground Glass Opacity

(incidental rib fracture)

SBRT 12.5 Gy X 4

6 month CT
Ground Glass Opacity with Reticular Consolidation

SBRT 12 Gy X 4

6 month CT
Radiation Fibrosis

SBRT 12 Gy X 4

16 month CT
Mass-like Fibrosis

SBRT 18 Gy X 3

18 month CT
Follow-up Imaging
Identifying Recurrence

- CT imaging
  - Increasing size/solidity after 12 months
- PET imaging (when CT is suspicious)
  - SUV > 5, at least 6 months after SBRT
  - Metabolic uptake has been seen out to 12 months post SBRT

Huang Radio Oncol 2012;102:335
Primary NSCLC

- Operable candidates should continue to receive surgical staging and resection (lobe or segment).
- Inoperable candidates with tumor < 5 cm should receive SBRT over standard fractionated EBRT.
- Inoperable candidate with tumor > 5 cm standard fractionated EBRT.
SBRT Current Indications

- Metastatic disease
  - Operable candidates should continue to receive surgical resection when indicated
  - Inoperable candidates who otherwise meet criteria for metastasectomy should consider SBRT.
SBRT Charge Capture

- CPT 32701
  - When planning in conjunction with a radiation oncologist
  - Medicare work RVU’s = 6.55
  - No global period (XXX)
  - No changes to radiation oncology billing
Conclusions

- Local control - ↑↑ with SBRT
- Distant metastases - now major obstacle
- Response assessment challenging
  - Tumor vs pneumonitis/fibrosis
- Appropriate post-SBRT imaging
  - Realistic assessment of salvage options
Image-guided Ablation Options

- Radiofrequency (RFA)
- Microwave (MWA)
- Laser (LA)
- Cryoablation (CA)
- Irreversible electroporation
Lung Ablation

- **Air:**
  - Insulator - high impedance

- **Vessels:**
  - Dissipates heat - protects normal tissue
  - Limits size of ablation margin
RFA

- Frictional heating - slow (6 min)
- Cell death at ≥ 60° C
- Zone of tissue necrosis
- ≥ 8 mm margin of groundglass*
- Heat sink

MWA

- Higher energy range than RF
- Larger achievable ablative zone
- More precise margins
- Faster treatment (2 min)
- Less heat sink effects

Brace et al. Radiology 2009; 251: 705–711
Eligibility
Patient Selection

- Stage IA NSCLC
- Refuse or cannot tolerate surgery
- Contraindication to RT
- Curative vs. palliative intent
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<th>Study</th>
<th>n</th>
<th>Size</th>
<th>1-yr Local Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akeboshi (2004)</td>
<td>54</td>
<td>&lt; 3 cm</td>
<td>69%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 3 cm</td>
<td>39%</td>
</tr>
<tr>
<td>Simon (2007)</td>
<td>18</td>
<td>≤ 3 cm</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>&gt; 3 cm</td>
<td>44%</td>
</tr>
<tr>
<td>Yamagami (2007)</td>
<td>82</td>
<td>≤ 2.5 cm</td>
<td>96%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 2.5 cm</td>
<td>62%</td>
</tr>
<tr>
<td>Gilliams (2008)</td>
<td>72</td>
<td>&lt; 3.5 cm</td>
<td>72%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 3.5 cm</td>
<td>0%</td>
</tr>
</tbody>
</table>
# Vessel Contact

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<tr>
<td></td>
<td></td>
<td>≥ 3.5 cm</td>
<td>0%</td>
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### Vessel Size

<table>
<thead>
<tr>
<th>Size</th>
<th>Local Control</th>
</tr>
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<tbody>
<tr>
<td>≤ 3 mm</td>
<td>77%</td>
</tr>
<tr>
<td>&gt; 3 mm</td>
<td>42%</td>
</tr>
</tbody>
</table>

*p = 0.04
Lesion Selection

- **Size:** $\leq 3$ cm
- **Size of pulmonary vessels in contact with lesion:** $\leq 3$ mm
- **Shape:** Round $> \text{Lobulated}$
- **Location:** Peripheral $> \text{Central}$
Lesion Selection

8 mm
Lesion Selection

Great candidate

Poor candidate

8 mm

43 mm
Lesion Selection

- ≤ 3 cm
- Round
- Central
- Contact with vessel > 3 mm
Complications
Stage IA NSCLC
Probe in place
Pneumothorax

0 - 60%
Probe in place
Hemorrhage
Hemoptysis

0 - 12%
## Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>&lt; Sublobar Resection</th>
<th>0-2.6%</th>
<th>0-5.3%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax</td>
<td>&lt; 40%</td>
<td>0-60%</td>
<td></td>
</tr>
<tr>
<td>Pneumothorax + chest tube</td>
<td>&lt; 15%</td>
<td>0-53%</td>
<td></td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>&lt; 5%</td>
<td>0-12%</td>
<td></td>
</tr>
<tr>
<td>Bronchopleural fistula</td>
<td>&lt; Sublobar resection</td>
<td>0-2%</td>
<td></td>
</tr>
<tr>
<td>30-day mortality</td>
<td>&gt; SBRT</td>
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<td>0-2.6%</td>
</tr>
<tr>
<td>90-day mortality</td>
<td></td>
<td></td>
<td>0-5.3%</td>
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Dupuy. Radiology 2011; 260: 633-655
Outcomes
Biases

- RFA patients are higher risk
- NO disease often not confirmed
- Little long term outcome data
- Few prospective trials
- No randomized controlled trials
## Stage IA Survival

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<tr>
<th>Study</th>
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<th>3y %</th>
<th>4y %</th>
<th>5y %</th>
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<tr>
<td>Dupuy-2006</td>
<td>24</td>
<td>92</td>
<td>62</td>
<td>55</td>
<td>49</td>
<td>46</td>
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<tr>
<td>Simon-2007</td>
<td>56</td>
<td>78</td>
<td>57</td>
<td>36</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>Wolf-2008</td>
<td>30</td>
<td>76</td>
<td>65</td>
<td>54</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Ambrogi-2011</td>
<td>59</td>
<td>87</td>
<td>71</td>
<td>49</td>
<td>33</td>
<td></td>
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### Stage IA NSCLC

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<tr>
<th>Tx</th>
<th>3-yr Local Control</th>
<th>3-yr Overall Survival</th>
<th>5-yr Overall Survival</th>
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<tbody>
<tr>
<td>Lob.</td>
<td>77-100%</td>
<td>61-98%</td>
<td>63-89%</td>
</tr>
<tr>
<td>SLR</td>
<td>72-100%</td>
<td>43-90%</td>
<td>48-71%</td>
</tr>
<tr>
<td>SBRT</td>
<td>50-100%</td>
<td>36-90%</td>
<td>30-53%</td>
</tr>
<tr>
<td>RFA</td>
<td>50-100%</td>
<td>36-90%</td>
<td>27-46%</td>
</tr>
<tr>
<td>No tx</td>
<td>16%</td>
<td></td>
<td>16%</td>
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Aggregate data 2002-2012
Imaging
Role of Imaging

Immediately after ablation:
- Adequacy of treatment
- Complications

Continuing:
- Local control
- Metachronous lesions
Ablation Changes

- Normal evolution:
  - Zone of ground glass opacity
  - Ablation zone enlargement
  - Tumor necrosis ± cavitation
  - Scar
Stage IA NSCLC

Preablation

Immediate post
Stage IA NSCLC

Preablation

3 months post
Complete Response

Preablation
Complete Response

3 mth post
Complete Response

6 mth post
Complete Response

9 mth post
Complete Response

12 mth post
Surveillance

Preablation
Surveillance

Preablation

6 mth post
Surveillance

6 mth post
Surveillance

6 mth post

Liver metastasis

PET-CT
Imaging Intervals

NO CONSENSUS RECOMMENDATIONS
Imaging Intervals

0 mths
CT

3 mths
CT

No imaging

6 mths
CT

9 mths
PET-CT

12 mths
CT
PET-CT

- May be performed at any time for suspect lesions
- Prior to 6 mths - cannot distinguish ablation from tumor
- 6 mth - predictive of response

Yoo et al. AJR 2001; 197: 334-340
Ablation Changes

- Enlargement in the treatment site beyond 6 months is indicative of residual disease/local failure

Bojarski et al. AJR 2005;185: 466–471
SBRT

- ≥ 3 cm in size
- Central location
- In contact with a vessel > 3 mm in diameter
- Lesion is biopsy proven NSCLC
Ablation

- ≤ 2 cm in size
- Peripheral
- No diagnosis (biopsy + RFA)
- Potential contraindication to RT
Conclusions
Conclusions

- Ablation is a treatment alternative in **select** medically inoperable patients
- Higher perioperative morbidity than SBRT
Conclusions

- Similar local control and overall survival as SBRT for lesions < 3 cm
- Patients with local failure can promptly be salvaged with SBRT or repeat ablation