Patterns of First Recurrence and Survival Comparison Between Surgical Resection and Stereotactic Radiation Therapy for Stage I Non-Small Cell Lung Cancer

Traves Crabtree MD, Varun Puri MD, Clifford Robinson MD, Jeffrey Bradley MD, Stephen Broderick MD, Alexander Patterson MD, Jingxia Liu PhD, Joann Musick RN, Jennifer Bell BSN, Michael Chang BS, Bryan Meyers MD
I am a consultant for Ethicon Endosurgery
Stage I NSCLC – Treatment Options

Medically operable

“High risk” operable (Z4099) (Z4032)

Medically inoperable

Surgery (lobectomy) CALGB ?

sublobar resection or SRT

SRT or RFA
# Patterns of Recurrence for SRT

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Median f/u</th>
<th>Overall Survival (OS)</th>
<th>Local failure</th>
<th>Regional Failure</th>
<th>Distant Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onishi 2004</td>
<td>245</td>
<td>24 mo</td>
<td>47% 5 yr OS</td>
<td>13.5%</td>
<td>8.2%</td>
<td>14.7%</td>
</tr>
<tr>
<td>Nyman 2006</td>
<td>45</td>
<td>43 mo</td>
<td>30% 5 yr OS</td>
<td>20%</td>
<td>4.4%</td>
<td></td>
</tr>
<tr>
<td>Lagerwaard 2008</td>
<td>206</td>
<td>12 mo</td>
<td>64% 2 yr OS</td>
<td>3%</td>
<td>9%</td>
<td>15%</td>
</tr>
<tr>
<td>Baumann 2008</td>
<td>60</td>
<td>23 mo</td>
<td>65% 2 yr OS</td>
<td>3.2%</td>
<td>3.2%</td>
<td>11.7%</td>
</tr>
<tr>
<td>Fakiris 2009</td>
<td>70</td>
<td>50 mo</td>
<td>42.7 3 yr OS</td>
<td>11.9%</td>
<td>8.6%</td>
<td></td>
</tr>
<tr>
<td>Ricardi 2010</td>
<td>62</td>
<td>28 mo</td>
<td>57.1% 3 yr OS</td>
<td>6.5%</td>
<td>12.9%</td>
<td>24.2%</td>
</tr>
<tr>
<td>Timmerman 2010</td>
<td>55</td>
<td>34 mo</td>
<td>55.8% 3 yr OS</td>
<td>7.3%</td>
<td>3.6%</td>
<td></td>
</tr>
<tr>
<td>Crabtree 2010</td>
<td>79</td>
<td>18 mo</td>
<td>32% 3 yr OS</td>
<td>11%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Andratschke 2011</td>
<td>92</td>
<td>21 mo</td>
<td>38% 3 yr OS</td>
<td>10.9%</td>
<td>18.5%</td>
<td></td>
</tr>
<tr>
<td>Senthi 2012</td>
<td>676</td>
<td>24 mo</td>
<td></td>
<td>4.9%</td>
<td>7.8%</td>
<td>14.7%</td>
</tr>
</tbody>
</table>
“…….we defined **local recurrence** after SRT as being within or adjacent to the primary tumor volume, and all other ipsilateral lung recurrences were classed as either distant recurrence or second primary tumours in the lung…….”

METHODS

• Retrospective study of all patients with Clinical Stage I NSCLC treated with SRT or Surgery from June 2004-Jul 2010

• Unmatched and matched comparisons of overall and disease-free survival, and freedom from local recurrence

• Patients from each cohort were propensity matched based on age, tumor stage, and ACE comorbidity index.
Local and Regional Recurrence Definitions for ACOSOG Z4099/RTOG 1021

• **Local failure**
  – Primary tumor failure
  – Marginal Failure
  – Involved lobe failure
  – Port site/wound recurrence

• **Regional failure**
  – Non-primary ipsilateral lobe failure
  – Hilar node failure
  – Ipsilateral mediastinal node failure
### UNMATCHED COMPARISON

<table>
<thead>
<tr>
<th>Variable</th>
<th>SRT</th>
<th>Surgery</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>151</td>
<td>458</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, Years (mean ± SD)</td>
<td>74.4 ± 9.4</td>
<td>65.8 ± 10.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male</td>
<td>53%</td>
<td>46.3%</td>
<td>0.1535</td>
</tr>
<tr>
<td>T2 lesions</td>
<td>27.2%</td>
<td>36%</td>
<td>0.0456</td>
</tr>
<tr>
<td>ACE Comorbidity Score 2-3</td>
<td>67.3%</td>
<td>35.9%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Surgical Procedure**

- Lobectomy: 75.8%
- Pneumonectomy: NA
- Bilobectomy: 3.7%
- Segmentectomy: 2.2%
- Wedge Resection: 7.6%
- Wedge Resection: 10.7%
Unmatched Comparison: Overall Survival

Surgery: 64% 5-yr OS

P < 0.0001

SRT: 25% 5-yr OS
Unmatched Comparison: Disease Free Survival

Surgery: 56% 5-yr DFS

SRT: 19% 5-yr DFS

P < 0.0001
Unmatched Comparison: Freedom From Local Recurrence

Surgery: 96% 5-yr FFLR

P<0.0001

SRT: 71% 5-yr FFLR
Pathologic Stage in Clinical Stage I Surgical Patients

- 11.8% pN1
- 3.0% pN2
- 3.1% pT3
- 2.2% pT4
- 18.4% of clinical T1 tumors found to be pT2

- 30-day mortality for surgery was 1.0% vs. 0.6% for the SRT cohort (p=NS)
## PROPENSITY MATCHED COMPARISON

<table>
<thead>
<tr>
<th>Variable</th>
<th>SRT</th>
<th>Surgery</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>83</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>Age, Years (mean ± SD)</td>
<td>71.5 ± 9.0</td>
<td>71.8 ± 8.2</td>
<td>0.9807</td>
</tr>
<tr>
<td>Male</td>
<td>50.6%</td>
<td>54.2%</td>
<td>0.6410</td>
</tr>
<tr>
<td>T2 lesions</td>
<td>26.5%</td>
<td>27.7%</td>
<td>0.8614</td>
</tr>
<tr>
<td>ACE Comorbidity Score 2-3</td>
<td>68.7%</td>
<td>67.5%</td>
<td>0.8678</td>
</tr>
</tbody>
</table>

### Surgical Procedure

- **Lobectomy**
  - SRT: 77.1%
- **Pneumonectomy**
  - SRT: 2.4%
- **Bilobectomy**
  - SRT: 0
- **Segmentectomy**
  - SRT: 6.0%
- **Wedge Resection**
  - SRT: 14.5%
Propensity Matched Comparison: Overall Survival

Surgery: 55% 5-yr OS

SRT: 29% 5-yr OS

P < 0.0004
Propensity Matched Comparison: Disease Free Survival

Surgery: 47% 5-yr DFS

SRT: 21% 5-yr DFS

P<0.0002
Propensity Matched Comparison: Freedom From Local Recurrence

Surgery: 97% 5-yr FFLR

SRT: 71% 5-yr FFLR

P=0.0109
Propensity Matched Comparison: Freedom From Regional Recurrence

SRT: 87% 5-yr FFRR

Surgery: 83% 5-yr FFRR

P = 0.9180
Propensity Matched Comparison: Freedom From Distant Recurrence

SRT: 58% 5-yr FFDR

Surgery: 78% 5-yr FFDR

P = 0.1551
SUMMARY

• In Stage I NSCLC patients matched for age, T stage, and ACE comorbidity, surgery offers better overall and disease-free survival, and lower local recurrence rates vs. SRT

• 38.5% of clinical stage I cancers were found to have a higher pathologic stage at surgery with occult nodal disease in 15%
CONCLUSIONS

• Current comparative studies are limited because of difficulty matching patients
• Recurrence patterns and survival do NOT justify routine use of SRT in low risk operable patients
• Current data are inadequate to define the role of SRT and surgery in high risk patients
Patterns of First Recurrence and Survival Comparison Between Surgical Resection and Stereotactic Radiation Therapy for Stage I Non-Small Cell Lung Cancer

THANK YOU!
Patterns Of Disease Recurrence Following Either Stereotactic Ablative Radiotherapy (sabr) Or Lobectomy By Video-assisted Thoracoscopic Surgery (vats) In Stage I-II Non-small Cell Lung Cancer: Outcomes Of A Propensity Score-matched Analysis

S. Senan¹, N. Verstegen¹, D. A. Palma², G. Rodrigues², F. J. Lagerwaard¹, A. van der Elst³, R. Mollema⁴, A. Warner², B. J. Slotman¹, J. W. Oosterhuis¹, ¹VU University Medical Center, Amsterdam, Netherlands, ²London Regional Cancer Program, London, ON, Canada, ³Department of Surgery, Spaarne Hospital, Hoofddorp, Netherlands, ⁴Department of Surgery, Medical Center Alkmaar, Alkmaar, Netherlands

• In total 86 VATS- and 527 SABR patients were eligible for matching
• The matched cohort consisted of patients with cT1-3N0 NSCLC following SABR (n=64) or VATS-lobectomy (n=64).
• Pre-treatment histological confirmation of stage I NSCLC was available in 53% of SABR patients and 50% of VATS patients
• SABR patients had a better loco-regional control rates at 1- and 3-years (96.8% and 93.3% vs. 86.9% and 82.6%, respectively, p= .03).
• Three-year progression-free survival did not significantly differ between groups (79.3% versus 63.2%, p = .09).

SBRT for Inoperable Early Stage Lung Cancer: RTOG 0236
Timmerman et al. JAMA 2010

• 55 inoperable pts. 80% T1.

• Primary endpoint: Primary tumor control
  – Primary tumor failure defined as local enlargement at least 20% by CT AND evidence of tumor viability based on PET
  – Recurrence within the lobe >1cm away from the primary tumor was NOT a primary tumor failure
  – Local failure defined separately

• 3-year primary tumor control 97.6%
## Metachronous Primary Lung Cancers after Treatment of Stage I Lung Ca

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Median F/U</th>
<th>Local failure</th>
<th>Distant Mets</th>
<th>Metachronous Primary</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRT (Onishi 2010)</td>
<td>87</td>
<td>55 mo</td>
<td>24.1%</td>
<td>21.8%</td>
<td>0</td>
</tr>
<tr>
<td>SRT (Bradley 2010)</td>
<td>91</td>
<td>18 mo</td>
<td>7.7%</td>
<td>20.8%</td>
<td>16.5%</td>
</tr>
<tr>
<td>Surgery (Flores 2011)</td>
<td>590</td>
<td>24 mo</td>
<td>4%</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Surgery (Martini 1995)</td>
<td>598</td>
<td>7 yrs</td>
<td>27%</td>
<td></td>
<td>7.5%</td>
</tr>
</tbody>
</table>
Stage I NSCLC – Treatment Options According to Some Radiation Oncologists

- Medically operable
- “High risk” operable
- Medically inoperable

SRT
Stage I NSCLC – Treatment Options According to Some Surgeons

Medically operable

“High risk” operable

Medically inoperable

SURGERY
Stage I NSCLC – Treatment Options

Medically operable

“High risk” operable

Medically inoperable

Surgery (lobectomy)

Sublobar resection or SRT

SRT or RFA