Endobronchial Ultrasound (EBUS)

Kazuhiro Yasufuku MD, PhD, FCCP
Director, Interventional Thoracic Surgery Program
Assistant Professor, University of Toronto
Division of Thoracic Surgery, Toronto General Hospital
Disclosure

• Industry-sponsored grants
  • Educational and research grants from Olympus Medical Systems Corp.

• Consultant for Olympus America Inc.

• Consultant for Intuitive Surgical Inc.
Mediastinal Staging

Clinical Staged, By cN

Pathologically Staged, By pN

<table>
<thead>
<tr>
<th></th>
<th>1 Yr</th>
<th>5 Yrs</th>
<th>HR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>cN0</td>
<td>84%</td>
<td>50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cN1</td>
<td>77%</td>
<td>39%</td>
<td>1.37</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>cN2</td>
<td>71%</td>
<td>31%</td>
<td>1.24</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>cN3</td>
<td>63%</td>
<td>21%</td>
<td>1.31</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>1 Yr</th>
<th>5 Yrs</th>
<th>HR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN0</td>
<td>86%</td>
<td>56%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pN1</td>
<td>77%</td>
<td>38%</td>
<td>1.63</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>pN2</td>
<td>69%</td>
<td>22%</td>
<td>1.51</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>pN3</td>
<td>49%</td>
<td>6%</td>
<td>1.81</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Rusch et al, J Thorac Oncol 2007;7:603
Mediastinal Staging

• Non-invasive staging (Imaging)
  • CT, PET-CT

• Invasive staging (Tissue diagnosis)
  • Surgical biopsy (Med, VATS)
  • Needle biopsy (TBNA, EBUS-TBNA, EUS-FNA, TTNA)
Endoscopic Staging - EBUS-TBNA

- Access to all LN stations accessible by Med as well as N1 nodes
- A minimally invasive modality
- Sensitivity 85-96%
- Real time procedure
- Doppler mode enables differentiation of LN from vessels
- Adopted in over 2500 centers
Convex Probe EBUS (CP-EBUS)

Outer Diameter: 6.9 mm
Scanning Range: 50 degrees
Instrument Channel: 2.2 mm
Optics: 35 degrees forward oblique

Division of Thoracic Surgery
Toronto General Hospital
Convex Probe EBUS (CP-EBUS)
Ultrasound Scanner - EU-C60, EU-ME1
NA-201SX-4022, 4021
EBUS-TBNA
Rapid On-site Evaluation (ROSE)
Rapid Feedback
Cell blocks often contain a “mini-core” of tumour.

Can be used for multiple immunohistochemical stains.

Can provide prognostic information (cell-cycle proteins, EGFR mutation).
EBUS-TBNA – Yield 10 studies (n=817)

• EBUS-TBNA Systematic Review and Meta-analysis
• Sensitivity = 0.88 (95%CI, 0.79-0.94), Specificity = 1.00 (95%CI, 0.92-1.00)
• Results compare favorably with published results for PET and CT

<table>
<thead>
<tr>
<th>Paper</th>
<th>Eligible patients (n)</th>
<th>Patient population</th>
<th>Inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Okamoto (2002)</td>
<td>37</td>
<td>Suspected lung cancer</td>
<td>ND</td>
</tr>
<tr>
<td>Yasufuku (2005)</td>
<td>108</td>
<td>Known/suspected lung cancer</td>
<td>CT mediastinal lymph nodes &gt; 1 cm on short axis</td>
</tr>
<tr>
<td>Rintoul (2005)</td>
<td>20</td>
<td>Known/suspected lung cancer</td>
<td>CT mediastinal lymph nodes &gt; 1 cm on short axis</td>
</tr>
<tr>
<td>Yasufuku (2006)</td>
<td>102</td>
<td>Known/suspected lung cancer</td>
<td>Stage I-IIIa</td>
</tr>
<tr>
<td>Plat (2006)</td>
<td>33</td>
<td>Suspected lung cancer</td>
<td>PET positive mediastinal lymph nodes</td>
</tr>
<tr>
<td>Pierard (2006)</td>
<td>51</td>
<td>Suspected lung cancer</td>
<td>PET positive mediastinal lymph nodes</td>
</tr>
<tr>
<td>Herth (2006)</td>
<td>100</td>
<td>Known NSCLC</td>
<td>CT mediastinal lymph nodes &lt; 1 cm on short axis</td>
</tr>
<tr>
<td>Yasufuku (2007)</td>
<td>45</td>
<td>Known/suspected lung cancer</td>
<td>Operable disease</td>
</tr>
<tr>
<td>Skwarski (2007)</td>
<td>300</td>
<td>Known/suspected lung cancer</td>
<td>ND</td>
</tr>
<tr>
<td>Annema (2007)</td>
<td>21</td>
<td>Known NSCLC</td>
<td>ND</td>
</tr>
</tbody>
</table>

ND, not described; NSCLC, non-small cell lung cancer; PET, positron emission tomography.

Adams et al. Thorax; 2009; 64: 757-62
Lung ca staging (N1 disease)

- NSCLC with hilar adenopathy or PET +ve LNs (n=188)
  - 229 LNs sampled
  - N3 (n=25), N1 (multiple n=40, single n=123)
  - Overall sensitivity 91%, specificity 100%
  - EBUS-TBNA of enlarged hilar lymph visible on CT or hilar nodes that are PET scan-positive can provide diagnostic results similar to those for central mediastinal nodes
  - Raises the possibility of neo-adjuvant tx

Lung ca staging (EBUS vs Med)

- Prospective cross-over trial (Ernst et al)
  - n=66, prevalence of malignancy 89%
  - Disagreement in the yield for #7 (24%; $p=0.011$).

- Prospective controlled study (Yasufuku et al)
  - n=153, operable patients
  - No difference between EBUS and Med

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Number</th>
<th>Prevalence of N2/N3</th>
<th>Sensitivity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ernst et al</td>
<td>2008</td>
<td>66</td>
<td>89</td>
<td>EBUS: 87</td>
<td>Med: 68</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EBUS: 78</td>
<td>Med: 59</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EBUS: 91</td>
<td>Med: 90</td>
</tr>
</tbody>
</table>

Cost Effectiveness

• A decision-tree analysis to compare downstream costs of EBUS-TBNA, conventional TBNA and mediastinoscopy.
  
  • **EBUS-TBNA (-ve results surgically confirmed) most cost-beneficial approach (AU$2961)**
  
  • EBUS-TBNA (-ve results not surgically confirmed) ($3344)
  
  • Conventional TBNA ($3754)
  
  • Mediastinoscopy ($8859)

Technical Aspects
# Standard EBUS Image Classification

<table>
<thead>
<tr>
<th>Size</th>
<th>Shape</th>
<th>Margin</th>
<th>Ecogenecity</th>
<th>Central Hilar Structure</th>
<th>Coagulation Necrosis Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) ≤ 1cm</td>
<td>(c) oval</td>
<td>(e) indistinct</td>
<td>(g) homogeneous</td>
<td>(i) present</td>
<td>(k) present</td>
</tr>
<tr>
<td>(b) &gt;1cm</td>
<td>(d) round</td>
<td>(f) distinct</td>
<td>(h) heterogeneous</td>
<td>(i) absent</td>
<td>(l) absent</td>
</tr>
</tbody>
</table>

How many aspirations

• How many aspiration per LN?
  • 102 NSCLC, 163 med LNs (Sensitivity 93.8%)
  • Maximum diagnostic values achieved in three aspirations
  • When at least one tissue-core specimen is obtained by the first or second aspiration, two aspirations per LN station can be acceptable

• How many LN stations per patient?
  • 92 NSCLC, 271 med LNs (2.9 per patient)
  • In 15 patients (60%), mediastinal disease was detected in the first station sampled; three samples were required to detect 90% of disease
  • Routinely sampling more than two mediastinal stations may improve staging

Lee et al. Chest. 2008;134: 368-74
21G or 22G?

Comparison of 21-gauge and 22-gauge aspiration needle during endobronchial ultrasound-guided transbronchial needle aspiration

Takahiro Nakajima, Kazuhiro Yasufuku, Ryo Takahashi, Masato Shingyoji, Tetsushi Hirata, Makiko Itami, Yukiko Matsui, Meiji Itakura, Toshihiko Iizasa and Hideki Kimura

- Comparison of 21G and 22G during EBUS-TBNA
  - No differences in the diagnostic yield
  - Histological structure more preserved in some samples
  - More blood contamination in 21G samples

Nakajima T et al, Respirology. 2011; 16(1): 90-4
Suction or no suction

• Transbronchial needle aspiration
Suction or no suction – Randomized trial

• **EBUS-TBNA** vs **EBUS-TBNCS** (EBUS-guided transbronchial needle capillary sampling)
• N=115,192 LNs
• Regardless of LN size, no differences in adequacy, diagnosis, and quality of samples
• There is no evidence of benefit of the practice of applying suction to EBUS-guided biopsies

*Casal RF et al, Chest. 2011Dec 8. [Epub ahead of print]*
Suction or no suction

- My current practice (unpublished)
  - Use Doppler mode to evaluate vascularity within all LNs
  - Start with suction
  - If aspirate is bloody, repeat procedure without suction
  - For subcarinal LN with higher vascularity, start without suction
Summary

- EBUS-TBNA is a novel approach that is safe and with a good diagnostic yield

- Access to all LN stations accessible by Med as well as the hilar LN

- EBUS-TBNA is less invasive, more safer and as accurate as surgical staging in NSCLC patients with discrete mediastinal lymph node enlargement.
Division of Thoracic Surgery
Toronto General Hospital
University Health Network

Kazuhiro Yasufuku, MD, PhD, FCCP
kazuhiro.yasufuku@uhn.ca

Thank you