Lung Cancer Staging

Endoscopic ultrasound (EUS) and Endobronchial ultrasound (EBUS)

Dr. Yuk Tong LEE
MBChB, MD(CUHK), FRCP (Edin), FRCP(Lond), FHKCP, FHKAM
Specialist in Gastroenterology and Hepatology
About 60% of all lung cancer cases are presented at advanced stage
Non-small cell lung cancer (NSCLC)

- 75-85% of all lung cancer cases
- Stage IIIB (T4, or N3) – five year survival 7-9%.
- Stage IIIA (N2 - Ipsilateral mediastinal, subcarinal) – five year survival 19-24%, Usually requires chemoRT before surgery
- National Cancer Institute and the Surveillance, Epidemiology and End Report – when NSCLC being diagnosed, 38% of the patient would have stage IIIa disease due to N2 LN met.
Irresectable tumor: T4, N3, M1

Accurate (mediastinal) staging is important to future management

<table>
<thead>
<tr>
<th>Stage IV</th>
<th>M1 (any T, any N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage III B</td>
<td></td>
</tr>
<tr>
<td>N3</td>
<td></td>
</tr>
<tr>
<td>Stage III A</td>
<td></td>
</tr>
<tr>
<td>N2</td>
<td></td>
</tr>
<tr>
<td>Stage II A</td>
<td>Stage II B</td>
</tr>
<tr>
<td>N1</td>
<td></td>
</tr>
<tr>
<td>Stage I A</td>
<td>Stage I B</td>
</tr>
<tr>
<td>N0</td>
<td></td>
</tr>
</tbody>
</table>

**Metastases (M)**

- **M0**: Absent
- **M1**: Present

Separate metastatic tumor nodule(s) in the ipsilateral nonprimary-tumor lobe(s) of the lung also are classified M1

**Tis**: Carcinoma in situ

Staging is not relevant for Occult Carcinoma (Tx, N0, M0)

- Including direct extension to intrapulmonary nodes
- Including superior sulcus tumor

<table>
<thead>
<tr>
<th>Local Invasion</th>
<th>Bronchial location</th>
<th>No invasion proximal to the lobar bronchus</th>
<th>Main bronchus (≥ 2 cm distal to the carina)</th>
<th>Main bronchus (&lt; 2 cm distal to the carina)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atelectasis/obstructive pneumonitis that extends to the hilar region but doesn’t involve the entire lung</td>
<td>Chest wall **/diaphragm/mediastinal pleura/parietal pericardium</td>
<td>Mediastinum/trachea/heart/great vessels/esophagus/vertebral body/carina</td>
<td>Malignant pleural/peri-cardial effusion or satellite tumor nodule(s) within the ipsilateral primary-tumor lobe of the lung</td>
<td>**</td>
</tr>
<tr>
<td>TNM6</td>
<td>TNM7</td>
<td>N0 Stage</td>
<td>N1 Stage</td>
<td>N2 Stage</td>
</tr>
<tr>
<td>----------</td>
<td>--------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>T1 (&lt;2 cm)</td>
<td>T1a</td>
<td>IA</td>
<td>IIA</td>
<td>IIIA</td>
</tr>
<tr>
<td>T1 (2–3 cm)</td>
<td>T1b</td>
<td>IA</td>
<td>IIA</td>
<td>IIIA</td>
</tr>
<tr>
<td>T2 (3–5 cm)</td>
<td>T2a</td>
<td>IB</td>
<td>IIA (IIB)</td>
<td>IIIA</td>
</tr>
<tr>
<td>T2 (5–7 cm)</td>
<td>T2b</td>
<td>IIA (IB)</td>
<td>IIB</td>
<td>IIIA</td>
</tr>
<tr>
<td>T2 (&gt;7 cm)</td>
<td>T3</td>
<td>IIB (IB)</td>
<td>IIIA (IIB)</td>
<td>IIIA</td>
</tr>
<tr>
<td>T3 (invasion)</td>
<td></td>
<td>IIB</td>
<td>IIIA (IB)</td>
<td>IIIA</td>
</tr>
<tr>
<td>T4 (nodules same lobe)</td>
<td></td>
<td>IIB (IIB)</td>
<td>IIIA (IIB)</td>
<td>IIIA (IIB)</td>
</tr>
<tr>
<td>T4 (extension)</td>
<td>T4</td>
<td>IIIA (IIB)</td>
<td>IIIA (IIB)</td>
<td>IIIA</td>
</tr>
<tr>
<td>M1 (ipsilateral lung)</td>
<td></td>
<td>IIIA (IV)</td>
<td>IIIA (IV)</td>
<td>IIIB (IV)</td>
</tr>
<tr>
<td>T4 (pleural effusion)</td>
<td>M1a</td>
<td>IV (IIIB)</td>
<td>IV (IIIB)</td>
<td>IV (IIIB)</td>
</tr>
<tr>
<td>M1 (contralateral lung)</td>
<td></td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
</tr>
<tr>
<td>M1 (distant sites)</td>
<td>M1b</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
</tr>
</tbody>
</table>

Shaded areas are changes in classification of early stage NSCLC.
Lung Cancer Staging Affects Treatment Option

<table>
<thead>
<tr>
<th>Staging</th>
<th>5-year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>58-73% (After surgery)</td>
</tr>
<tr>
<td>1b</td>
<td>43-58%</td>
</tr>
<tr>
<td>IIa</td>
<td>36-46% (After surgery)</td>
</tr>
<tr>
<td>IIb</td>
<td>25-36%</td>
</tr>
<tr>
<td>IIIA</td>
<td>19-24% (After surgery)</td>
</tr>
<tr>
<td>IIIB</td>
<td>7-9%</td>
</tr>
<tr>
<td>IV</td>
<td>2-13%</td>
</tr>
</tbody>
</table>

Resectable vs. Irresectable

Chemotherapy and Radiotherapy

Accessed 31 March, 2011

Consequence of wrong staging

False +ve staging (Up stage)
- Patient being declined curative surgery

False –ve staging (down stage)
- Patient received invasive futile surgery
- Increased morbidity and mortality
- Missed a chance to receive neoadjuvant chemoRT
Staging methods for mediastinal LN (MLN)

- Non-invasive staging
  - CT scan
  - PET scan

- Invasive staging
  - EUS-FNA
  - EBUS-FNA
  - Mediastinoscopy
  - VATS
Noninvasive staging

- Meta-analysis

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Sen</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>3438</td>
<td>57%</td>
<td>82%</td>
<td>56%</td>
<td>83%</td>
</tr>
<tr>
<td>PET</td>
<td>1045</td>
<td>84%</td>
<td>89%</td>
<td>79%</td>
<td>93%</td>
</tr>
</tbody>
</table>

Toloza EM, Chest 2003
CT scan

- CT +ve MLN – 44% false +ve
- CT normal mediastinum, N1 node enlargement – MLN (N2,3) metastases 20-25% (false –ve)
- CT peripheral stage I tumour, incidence of N2,3 disease (<10%)

PET staging

- +ve PET/CT - enlarged LN – false +ve 21%
  normal size LN – false +ve 50%
- -ve PET/CT - normal size LN – false –ve 9%
  enlarged nodes – false –ve 10%.

- False -ve PET - 20–30% in enlarged MLN
  and 25% in normal mediastinum and enlarged N1 nodes.

- For patients with a peripheral clinical stage I tumour,
  false –ve PET <5%.

Tissue is the issue!

Invasive staging of lung cancer

**Meta-analysis**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Study no./ N</th>
<th>Sen</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBNA</td>
<td>17 / 1339</td>
<td>78%</td>
<td>99%</td>
<td>99%</td>
<td>72%</td>
</tr>
<tr>
<td>TTNA</td>
<td>5 / 215</td>
<td>89%</td>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>16 / 1003</td>
<td>84%</td>
<td>99.5%</td>
<td>99.3%</td>
<td>81%</td>
</tr>
<tr>
<td>EBUS-FNA</td>
<td>8 / 918</td>
<td>90%</td>
<td>100%</td>
<td>100%</td>
<td>80%</td>
</tr>
<tr>
<td>Cervical mediastinoscopy</td>
<td>19 / 6505</td>
<td>78%</td>
<td>100%</td>
<td>100%</td>
<td>89%</td>
</tr>
<tr>
<td>VATS</td>
<td>7 / 419</td>
<td>75%</td>
<td>100%</td>
<td>100%</td>
<td>93%</td>
</tr>
</tbody>
</table>

Detterbeck FC, Chest 2007
Endoscopic Ultrasonography (EUS) and Endobronchial Ultrasonography (EBUS)

- Both showed high sensitivity in detecting mediastinal lymph nodes
- Could perform fine needle aspiration or trucut biopsy (EUS)
- Comparable to surgical staging method
Linear EUS

- Scanning plane is along the scope shaft
- Blood flow study
- Guided FNA

Needle

Tumour
Endobronchial ultrasound (EBUS)

- Working channel (2.0mm)
- 7.5 MHz Convex
- Optical system
- Forward oblique
- Shaft (6.9mm)

Vessel
LN
Mediastinal LN stations

- American Joint Committee on Cancer (AJCC) and American Thoracic Society (ATS) classification
Mediastinal lymph node station

Accessibility by EUS and EBUS

- EUS – 2L, 3P, 4L, (5, 6), 7, 8, 9, 10R/10L

- EBUS – 2R/2L, 4R/4L, 7, 10, 11, 12

Lee YT, Gastrointest Endosc 2009
Station 8, 9
Subcarinal Lymph Node

Pulmonary Artery

Thrombus

EUS

FNA

Subcarinal Lymph Node

Pulmonary Artery

thrombus
Station 4L, 5
Station 4L, 5

4L LN

Pulmonary artery

Aorta

ligamentum arteriosum

Lee YT, Gastrointest Endosc 2009
Superior mediastinum

3A

3P

2R

2L
Intraabdominal station

- Celiac artery, celiac lymph node
- Left adrenal gland
**EUS-FNA for CT +ve MLN**

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>153</td>
<td>95%</td>
<td>92%</td>
<td>100%</td>
</tr>
<tr>
<td>Without cancer</td>
<td>101</td>
<td>94%</td>
<td>88%</td>
<td>100%</td>
</tr>
<tr>
<td>With cancer</td>
<td>52</td>
<td>98%</td>
<td>97%</td>
<td>100%</td>
</tr>
</tbody>
</table>

- In 19 (12%) patient, CT did not detect the LN
- No statistical difference in size, location and morphology between the benign and malignant LN
- In 9/52 (17%) patient with previous cancer, second cancers were found

Fritscher-Ravens A. Am J Gastroenterol 2000
EUS-FNA for CT -ve MLN

- N = 277
- EUS-FNA detected stage III/IV disease in 70%
- CT +ve MLN: 75/97 (77%) had stage III/IV detected by EUS
- CT –ve MLN: 10/24 (42%) had stage III/IV detected by EUS
- Specificity for MLN met: CT 32% vs EUS 100%

- EUS should be considered a first line method of pre-surgical evaluation of patients with tumour of the lung

Wallace MB. Ann Thorac Surg 2002
EUS-FNA for CT-ve MLN

- 69 NSCLC and CT-ve MLN. EUS-FNA on at least one LN.
- EUS-FNA confirmed 14/69 malignant LN and 3/69 stage III/IV
- Altered management in 25% of patients.
- The sensitivity of EUS for advanced mediastinal disease was 61% (49% to 75%), and the specificity was 98% (95% to 100%).

Wallace MB. Ann Thorac Surg 2004
EUS-FNA following CT/PET staging

- 104 patients
- +ve MLN: PET (SUV ≥ 2.5), or CT (LN ≥ 1cm in the short axis)
- 125 lesions (117 lymph nodes, 8 left adrenal glands)

<table>
<thead>
<tr>
<th></th>
<th>Sen</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
<th>Accu</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td></td>
<td></td>
<td>39.2%</td>
<td></td>
<td>40.3%</td>
</tr>
<tr>
<td>PET</td>
<td></td>
<td></td>
<td>40.3%</td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>EUS</td>
<td>80%</td>
<td>62.5%</td>
<td>57.2%</td>
<td>83.3%</td>
<td>69.2%</td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>92.5%</td>
<td>100%</td>
<td>100%</td>
<td>95.5%</td>
<td>97.1%</td>
</tr>
</tbody>
</table>

- EUS-FNA vs PET or CT: Accuracy and PPV ($p < 0.001$)
- EUS-FNA confirmed 4 left adrenal met.

Eloubeidi MA, Ann Thorac Surg 2005
EUS-FNA for centrally located tumour

- Non-diagnostic bronchoscopy up to 30% of cases.
- 32 patient with centrally located lung mass and non-diagnostic bronchoscopy.
- Diameter of masses 45mm (range 15—90mm)
- No MLN enlargement
- EUS-FNA diagnosed cancer in 31 of 32 patients (97%). One -ve FNA was later shown to be lymphoma by pneumonectomy.
- 13 (41%) patients were staged T4 diseases – no operation
- No complications occurred.

Annema JT, Lung Cancer 2005
EUS-FNA for mediastinal staging

- N=120, suspected thoracic malignancy.
- -ve EUS-FNA was followed by surgical staging.
- 120 EUS-FNA, 53 mediastinoscopy and 48 open lymphadenectomies
- Dx: Lung carcinoma (99), lung metastases (6), mesothelioma (5), lymphoma (3), other conditions (8).
- EUS: T4 (15) and adrenal or hepatic metastases in (9)
- Prevalence of MLN metastases - 51.7%.
- EUS-FNA: False -ve 25.3%.

71 (59%) patients impacted on management, without surgical staging, 20.8% inadequate therapy

EUS-FNA as the first test for lung mass

- Multiple tests are required for the management of lung cancer.
- EUS-FNA a single test for the diagnosis and staging of lung cancer?
- 113 patients with lung mass on CT.
- EUS performed right after CT scan in 93 (82%) cases.
- EUS-FNA established tissue diagnosis in 70% of cases.
- Accuracy of diagnosing MLN metastases (n=49):
  - EUS-FNA (93%), CT (81%), and PET (93%)

Singh P, Am J Respir Crit Care Med 2007
EUS-FNA as the first test for lung mass

- Liver met (n=13): EUS-FNA +ve in 11.
- Left adrenal met (n= 15): EUS-FNA +ve in 14.
- Celiac axis LN met: 11% of cases – poor prognosis.
- Accuracy of CLN met: EUS-FNA (100%) vs CT (50%) (p<0.05).
- The median survival: EUS CLN +ve 142.5D vs EUS CLN –ve 330D (p<0.002)
- Overall 40 metastatic lesions were detected in the liver, adrenal gland, and celiac axis in 32 patients with distant metastases.
  - Sensitivity EUS-FNA (93%), CT (80%), and PET (50%)
- 44 cases with resectable tumor on CT scan, EUS-FNA avoided thoracotomy in 14% of cases

Singh P, Am J Respir Crit Care Med 2007
Adrenal and liver metastases
EUS-FNA for staging of N2/3 MLN: meta-analysis

- 18 eligible studies
- EUS-FNA – pooled sensitivity 83%, specificity 97%
- In CT +ve MLN, 8 studies, pooled sensitivity 90%, specificity 97%
- In CT –ve MLN, 4 studies, pooled sensitivity 58%.
  - (35% prevalence of malignant MLN)
- Minor complications 0.8%, no major complications.
- No significant heterogeneity among studies.

Micames CG, Chest 2007
EUS and EUS-FNA for mediastinal lymphadenopathy: Metaanalysis

- 76 studies (n = 9310)
- 44 studies EUS alone and 32 EUS-FNA

**Sensitivity**
- EUS (84.7%)
- EUS-FNA (88.0%)

**Specificity**
- EUS (84.6%)
- EUS-FNA (96.4%)

No publication bias

Puli SR, World J Gastroenterol 2008
PWH experience

- July 1998 to June 2007, 125 patients with mediastinal LN or masses,
- Total 130 EUS-FNA.
- Median age 69 years old (range 31 - 90), male 76%.

Lee YT, Hong Kong Med J 2010
## Result of EUS-FNA

<table>
<thead>
<tr>
<th>Confirmed Cancer</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Confirmed Cancer</strong></td>
<td><strong>62 (49.6%)</strong></td>
</tr>
<tr>
<td>Primary Lung Cancer</td>
<td></td>
</tr>
<tr>
<td>NSCLC</td>
<td>44</td>
</tr>
<tr>
<td>SCLC</td>
<td>11</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Malignant GIST</td>
<td>1</td>
</tr>
<tr>
<td>Lymphoma (+ HCC confirmed by EUS-FNA)</td>
<td>1</td>
</tr>
<tr>
<td>Metastatic Lung Cancer</td>
<td></td>
</tr>
<tr>
<td>Renal Cell Carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Adenocarcinoma from small bowel</td>
<td>1</td>
</tr>
<tr>
<td>Prostatic Cancer</td>
<td>1</td>
</tr>
<tr>
<td>Bone Cancer</td>
<td>1</td>
</tr>
<tr>
<td>Confirmed Benign</td>
<td><strong>42 (33.6%)</strong></td>
</tr>
</tbody>
</table>

Lee YT, Hong Kong Med J 2010
Outcome

- Eighty-six (68.8%) patients had altered their initial plan of management.
- Favour non-surgical or palliative treatment.

Lee YT, Hong Kong Med J 2010
Could EUS-FNA reduce futile surgery?

- 242 patients: suspected (n=142) or proven (n=100) lung cancer
- CT - enlarged (>1 cm) mediastinal LNs
- Plan for mediastinoscopy/tomy (94%) or exploratory thoracotomy (6%). Before surgery, EUS-FNA was done.

- EUS-FNA: Prevented 70% of scheduled surgery
  - LN metastases in NSCLC (52%)
  - tumor invasion (T4) (4%),
  - tumor invasion and LN metastases (5%)
  - SCLC (8%)
  - Benign diagnoses (1%).

- EUS-FNA: sensitivity (91%), specificity (100%), and accuracy (93%)

- No complication

Annema JT, J Clin Oncol 2005
EBUS-FNA: CT +ve MLN

- 108 patient with known or suspected lung cancer
- CT scan showed enlarged mediastinal LN (>1cm)
- In 105 patients, EBUS-FNA was successfully performed to obtain samples from 163 lymph nodes.
- EBUS-FNA: Sensitivity of 94.6%, specificity of 100%, PPV 100%, NPV 89.5%, accuracy 96.3%.
- 29 mediastinoscopies, 8 thoracotomies, 4 thorascopies, and 9 CT-guided percutaneous biopsy were avoided.
- No complication.

Yasufuku K, Lung Cancer 2005
EBUS-FNA: CT +ve MLN

- 502 patients (mean age 59 (24-82) years), 572 LNs
- 535 (94%) resulted in a diagnosis
- Biopsies were taken from LN in region 2L, 2R, 3, 4R, 4L, 7, 10R, 10L, 11R and 11L
- Mean diameter of the nodes - 1.6 cm
- EBUS-FNA: Sensitivity 94%, specificity was 100%, PPV 100%.
- No complication

Herth FJ, Thorax  2006
EBUS-FNA in CT –ve LN

- NSCLC patients with CT scans showing no enlarged lymph nodes (no node > 1 cm) in the mediastinum
- 100 patients, 119 lymph nodes (5-10mm)
- Confirmed malignancy (by surgery) in 19 patients but missed in 2 others
- The mean diameter of the punctured LN - 8.1 mm.
- EBUS-FNA: sensitivity 92.3 %, the specificity 100%, NPV 96.3 %.
- No complication
- Unnecessary surgical exploration was avoided in 1/6 of patients who have no CT evidence of mediastinal disease

Herth FJ, Eur Respir J 2006
EBUS-FNA for centrally located tumour

- Retrospective analysis
- If EBUS-FNA –ve, proceed to transthoracic FNA or a surgical diagnostic procedure.
- 60 patients, 82% prior nondiagnostic bronchoscopy.
- Out-patient setting 97%
- Primary lung lesion was observed in all cases.
- EBUS-FNA confirmed lung cancer in 46 (77%).
- EBUS-FNA for diagnosing lung cancer – sen 82%, NPV 23%.
- TTNA or surgical staging was avoided in 47% and 30% of patients, respectively.
- No serious procedure-related complications

Tournoy KG, Lung cancer 2008
EBUS-FNA for recurrent lung cancer
EBUS-FNA vs EUS-FNA

- 160 patients with enlarged MLN (CT >1cm)
- A crossover design
- Excluded hilar nodes (station 5, 6, 11), and station 8, 9 nodes
- Success: EBUS-TBNA (88%), EUS-FNA (78%), combined (97%)
- Diagnosis: EBUS-TBNA (85%), EUS-FNA (76%), combined (94%)
- Procedure time: EBUS (3.2 min) vs EUS (4.1 min).
- The EBUS was superior in nodes 2R, 4R, and 10R. No complications
- Combining both approaches provides results similar those of mediastinoscopy.

Herth FJ, Am J Respir Crit Care Med 2005
EUS-FNA plus EBUS-FNA for mediastinal staging

- $N = 138$,
- TBNA vs EUS-FNA vs EBUS-FNA
- 42 (30%) had malignant LN
- PET sensitivity - 24%, CT sensitivity - 67%,
- Procedure duration (median, min):

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Sensitivity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBNA</td>
<td>15/42 (36)  [22-52]</td>
<td>96/123 (78) [70-85]</td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>29/42 (69)  [53-82]</td>
<td>96/109 (88) [80-93]</td>
</tr>
<tr>
<td>EBUS-FNA</td>
<td>29/42 (69)  [53-82]</td>
<td>96/109 (88) [80-93]</td>
</tr>
<tr>
<td>EUS-FNA + TBNA</td>
<td>33/42 (79)  [63-90]</td>
<td>96/105 (91) [84-96]</td>
</tr>
<tr>
<td>EBUS-FNA + TBNA</td>
<td>32/42 (76)  [61-88]</td>
<td>96/106 (91) [83-95]</td>
</tr>
<tr>
<td>EUS-FNA + EBUS-FNA</td>
<td>39/42 (93)  [81-99]</td>
<td>96/99 (97) [91-99]</td>
</tr>
</tbody>
</table>

Wallace MB. JAMA 2008
Medical (endoscopic) mediastinoscopy

**EBUS**
Anterior and superior mediastinum, anterior subcarina, hila of the lung

**EUS-FNA**
Posterior mediastinum, aortopulmonary window, posterior subcarina, lower pare-esophageal, celiac axis, left adrenal gland
Mediastinoscopy

Standard cervical mediastinoscopy:
- Sensitivity ~ 68-73%
- False –ve: 12-20%
- Station: 2R, 2L, 4R, 4L, 7 (anterior)
- Could not assess stations: 8, 9, 5, 6, 7 (posterior)
- Could not assess intraabdominal LN or left adrenal gland
- Major haemorrhage 0.4%, left recurrent laryngeal nerve palsy 1-2%.

Anterior mediastinoscopy:
- Sensitivity: 63-86%
- False –ve: 0-11%

Extended cervical mediastinoscopy:
- Sensitivity: 87%
- False –ve: 8-11%

## EUS/EBUS vs Mediastinoscopy

<table>
<thead>
<tr>
<th></th>
<th>EUS/EBUS</th>
<th>Mediastinoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>Outpatient</td>
<td>In-patient</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>half day</td>
<td>≥ 2 days</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>LA + IV sedation</td>
<td>GA</td>
</tr>
<tr>
<td>Accuracy</td>
<td>high</td>
<td>high</td>
</tr>
<tr>
<td>Complication</td>
<td>very low</td>
<td>Low (but serious)</td>
</tr>
<tr>
<td>Cost</td>
<td>$$</td>
<td>$$$$</td>
</tr>
</tbody>
</table>
# Accessible LN station by different procedure

<table>
<thead>
<tr>
<th>LN station</th>
<th>EUS–FNA</th>
<th>EBUS–TBNA</th>
<th>Cervical mediastinoscopy</th>
<th>Anterior mediastinotomy</th>
<th>Left-sided VATS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2R</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2L</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4R</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4L</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>10R</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>10L</td>
<td>+/-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>11R/11L</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Vansteenkiste J, Ann Oncol 2010
EUS-FNA added to mediastinoscopy

- Prospective, nonrandomized multicenter trial
- 107 consecutive potentially resectable NSCLC patients

For LN met, Combined (36%), mediastinoscopy (20%), EUS-FNA (28%).

This indicated that **16%** of thoracotomies could have been avoided by using EUS-FNA in addition to mediastinoscopy

Annema JT, JAMA 2005
EUS-FNA vs Mediastinoscopy

- N = 40
- 19 to EUS-FNA vs 21 to surgical mediastinal staging.
- EUS-FNA group, surgical staging was needed in 32%.
- Sensitivity for malignant LN: EUS-FNA 93% vs surgical staging 73% (P=0.29)
- Complication rate: EUS-FNA (0%) vs surgical staging (5%) (P=1.0).
- Median hospital stay EUS-FNA (0) vs surgical staging (2) (P<0.001)

Tournoy KG, Am J Respir Crit Care Med 2008
EUS/EBUS vs mediastinoscopy - complementary

First EUS (EBUS), if –ve, proceeds to mediastinoscopy

Or do both EUS (EBUS) and mediastinoscopy

Currently 5 randomization studies are going on (BOOST, ASTER, etc)
2. For patients with discrete mediastinal LN enlargement (and no distant metastases), invasive confirmation is recommended (regardless of PET scan result).

Grade of recommendation, 1B

3. Mediastinoscopy, EUS-FNA, TBNA, EBUS-FNA, or TTNA could be used to confirm N2,3 LN depending of expertise that available.

Grade of recommendation, 1B

4. A nonmalignant result from a needle technique (eg, EUS-FNA, TBNA, EBUS-FNA, or TTNA) should be further confirmed by mediastinoscopy.

Grade of recommendation, 1C
5. For patients with a normal CT mediastinum and a central tumor or N1 LN enlargement (and no distant metastases), invasive confirmation is recommended (regardless of PET scan result).

   Grade of recommendation, 1C

6. In general, mediastinoscopy is suggested, but EUS-FNA or EBUS-FNA may be a reasonable alternative if nondiagnostic results are followed by mediastinoscopy.

   Grade of recommendation, 2C
7. For patients with a peripheral clinical stage I tumor and PET +ve mediastinal LN (and not distant metastases), invasive staging is recommended. In general, mediastinoscopy is suggested, but EUS-FNA or EBUS-FNA may be a reasonable alternative if nondiagnostic results are followed by mediastinoscopy. 

Grade of recommendation, 1C
9. For patients with an LUL cancer, invasive mediastinal staging include assessment of the APW nodes (via Chamberlain procedure, thoracoscopy, extended cervical mediastinoscopy, EUS-FNA, or EBUS-FNA) is indicated.

Grade of recommendation, 2C
Algorithm for staging NSCLC (Simplified)

Lung mass

Bronchoscopy, CT-FNA

NSCLC

CT & PET – MLN, distant met

Stage 1
Surgery

Stage II & III?
Invasive staging

Stage IV (M1)
Palliation

EUS-FNA +/- EBUS-FNA for tissue diagnosis and staging

Stage IV (M1)
ChemoRT
Surgery

-ve
+ve N2/3
European Society of Thoracic Surgeons guidelines

- **CT-scan**
  - negative (N0)
  - positive (N2-N3)
    - tissue confirmation
      - (3) EBUS/EUS
        - negative
        - positive
          - mediastinoscopy
            - (4) negative
            - positive
              - multimodality treatment
              - upfront surgery
European Society of Thoracic Surgeons guidelines

PET/CT-scan

- negative (N0)
  - upfront surgery
- positive (N2-N3)
  - tissue confirmation
    - (1)
    - mediastinoscopy
      - positive
      - multimodality treatment
      - (2)
      - EBUS/EUS
        - negative
        - (3)
        - positive
  - (2)

Conclusion

- EUS-FNA and EBUS-FNA is a minimally invasive procedure for staging of lung cancer disease
- High diagnostic accuracy
- Low complication
- An important tool in triaging patient to receive appropriate therapy
- Should be included in the routine staging algorithm of lung cancer disease