Diagnosis and Staging of Lung Cancer: State-of-the-Art

Copicon Congress (SATS)
Durban 29 July 2011
CT Bolliger

University of Stellenbosch
Projected annual tobacco-related deaths

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>Developed countries</th>
<th>Developing countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>1950</td>
<td>300 000</td>
<td>300 000</td>
<td>Negligible</td>
</tr>
<tr>
<td>1965</td>
<td>1 000 000</td>
<td>900 000</td>
<td>100 000</td>
</tr>
<tr>
<td>1975</td>
<td>1 500 000</td>
<td>1 300 000</td>
<td>200 000</td>
</tr>
<tr>
<td>1995</td>
<td>3 000 000</td>
<td>2 000 000</td>
<td>1 000 000</td>
</tr>
<tr>
<td>2000</td>
<td>3 500 000</td>
<td>2 400 000</td>
<td>1 100 000</td>
</tr>
<tr>
<td>2025</td>
<td>10 000 000</td>
<td>3 000 000</td>
<td>7 000 000</td>
</tr>
</tbody>
</table>

McKay JL. *Tuber Lung Dis* 1994

Latest prediction: 1 Billion / 21st century
Diagnosis
• NSCLC
• SCLC

Stage
• I - IV TNM
• Limited / extensive

Function
• FEV$_1$
• DL$_{CO}$
• VO$_2$ max

15 - 25% operable
Clinico-pathological Staging

A: Imagery
- CXR
- CT scan
- PET-CT
- MR scan

B: Pathology (Invasive methods)
- Transthoracic needle aspiration (TTNA)
- Transbronchial needle aspiration (TBNA ± EBUS)
- Electromagnetic navigation
- Thoracoscopy
- Mediastinoscopy
- Mediastinotomy
PET scan

2-[18F]fluoro-2-deoxy-D-glucose (FDG)
Produced in cyclotron on site, half-life 110 min
Normal: Brain (B), heart (C), bladder (B). Abnormal: Tumor (T)
Integrated CT-PET

### Table 3. Diagnostic Accuracy of the Imaging Methods with Respect to Node Stage in 37 Patients.

<table>
<thead>
<tr>
<th>Imaging Method</th>
<th>Classification Correct (Score of 3)</th>
<th>Classification Correct but Equivocal (Score of 2)</th>
<th>Classification Incorrect (Score of 0 or 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT alone</td>
<td>22 (59)</td>
<td>2 (5)</td>
<td>13 (35)</td>
</tr>
<tr>
<td>PET alone</td>
<td>18 (49)</td>
<td>14 (38)</td>
<td>5 (14)</td>
</tr>
<tr>
<td>Visual correlation of PET and CT</td>
<td>22 (59)</td>
<td>4 (11)</td>
<td>11 (30)</td>
</tr>
<tr>
<td>Integrated PET–CT</td>
<td>30 (81)</td>
<td>1 (3)</td>
<td>6 (16)</td>
</tr>
</tbody>
</table>

Detection of extrathoracic metastases by emission tomography in lung cancer.

Unexpected ETM: 13/94 patients (14%)
Upstaged to N3: 6/94 patients (6%)

Understaged: 20% of patients

The use of PET–CT for preoperative staging of NSCLC reduced both the total number of thoracotomies and the number of futile thoracotomies but did not affect overall mortality.

Fischer B. NEJM 2009;361:32-39
PET summary

- High negative predictive value for of N2 or N3
  - Mediastinoscopy can be omitted if negative
  - Direct surgical resection after negative PET
- False positive findings occur
  - inflammatory nodes or granulomatous disorders
  - confirmation by mediastinoscopy mandatory
- Detects unexpected metastatic lesions
  - An isolated finding requires pathological verification

Vansteenkiste. Lung Cancer 2003;42:S27
Tissue is the issue: How?

- Bronchoscopy ± EBUS:
- EUS:
- Mediastinoscopy:
- VATS:

EBUS = Endobronchial Ultrasound, EUS = Esophageal US
The Nodes
Mediastinal LN – Methods and Reach

[Diagram showing various mediastinal nodes with different methods of sampling: Mediastinoscopy/EBUS-TBNA, EUS-FNA, Parasternal Mediastinotomy.

Annema JT 2005]
Bronchoscopic tools

● **Visualisation:**
  - White light (WLB)
  - AFB (increased sensitivity)
  - EBUS (beyond the visible: airway wall, LN, vessels)

● **Sampling:**
  - Wash
  - Brush
  - Forceps
  - TBNA
Beginner’s delight: Visible tumor Trachea: Stage IIIb
## Diagnostic Yield of Individual Bronchoscopic Procedures for Endoscopically Visible Lung Cancers

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. of Patients</th>
<th>Diagnosis</th>
<th>Average Diagnostic Yield (%)</th>
<th>Range(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW</td>
<td>1535</td>
<td>1041</td>
<td>68</td>
<td>27-90</td>
</tr>
<tr>
<td>BR</td>
<td>1578</td>
<td>1131</td>
<td>72</td>
<td>44-94</td>
</tr>
<tr>
<td>EBB</td>
<td>1934</td>
<td>2418</td>
<td>80</td>
<td>51-97</td>
</tr>
<tr>
<td>EBNA</td>
<td>456</td>
<td>365</td>
<td>80</td>
<td>68-91</td>
</tr>
</tbody>
</table>

BW = Bronchial Wash, BR = Brush, EBB = Endobronchial Biopsy
EBNA = Endobronchial Needle Aspiration

What we do: ROSE-TBNA

Rapid On Site Evaluation

- On-site staining of specimens
- Combines diagnosis and staging
- All patients for diagnostic work-up with solid lesions (malignant and benign)!!!
What we need: TBNA needles

- 22G or 21G or 20G for cytology
- 19G for histology
 ..........and: Chris‘ Angels
ROSE: personnel (min.4)
TBNA specimen preparation

- Immediately smear on slide and fix with cytospray
- Or: stain on site (ROSE)
- Alternative, not advised: Rinse into vial (poor yield)

Stain: Quick-PAP
Learned’s plight: T2, N0, M0 [stage Ib]?
CT Scan before Bronchoscopy!
T2, N2, M0 [stage IIIa]?
Know your anatomy!

ROSE TBNA of enlarged LN: stage IIIa !!!
EBUS or.....The move beyond the visible
No invasion – compression!
Ballooncatheter

- circular contact
- high resolution (20MHz)
- deep penetration
sterile water

connector to driving unit

transducer and balloon
Outer Diameter: 6.7mm
Scanning Range: 50 degrees
Instrument Channel: 2.2mm
Optics: 35 degrees forward oblique
Comparison of competing methods to sample neoplastic mediastinal lesions: 2005

- **ROSE-TBNA:** 77%
  - Diacon AH. Respiration 2005; 72: 182-8

- **ROSE-TBNA:** (36.7% remote) 70.6%
  - Napier MB. ATS 2005, A911

- **EBUS-TBNA:** 85%

- **EUS-FNA:** 78%

- **EBUS-TBNA+EUS-TBNA:** 94%
  - Herth FJF. AJRCCM 2005; 171: 1164-67
<table>
<thead>
<tr>
<th>Item Description</th>
<th>Quantity</th>
<th>Price (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 CT TBNA</td>
<td>100</td>
<td>65,500</td>
</tr>
<tr>
<td>100 EBUS/TBNA</td>
<td></td>
<td>53,300</td>
</tr>
<tr>
<td>100 MESK</td>
<td></td>
<td>150,000</td>
</tr>
</tbody>
</table>

Courtesy HD Becker, Heidelberg
Endobronchial Ultrasound-Guided TBNA of Lymph Nodes in the Radiologically and PET-Normal Mediastinum in Patients With Lung Cancer
Herth FJF, Eberhardt R, Krasnik M, Ernst A. CHEST 2008;133:887-91

- 97 patients (mean age, 52.9 years; 57 men), high suspicion of NSCLC with CT scans showing no enlarged lymph nodes (no node > 1 cm) and a neg. PET of the mediastinum
- EBUS-TBNA. Identifiable LN (2r, 2L, 4r, 4L, 7, 10r, 10L, 11r, 11L) All patients underwent subsequent surgical staging. Comparison between TBNA and surgical results.
- 156 LN (5-10 mm ø), Malignancy in 9, but missed in 1 patient. Mean diameter of the punctured lymph nodes was 7.9 mm. Sens.: 89%, spec.: 100%, NPP: 98.9%. No complications
- **In conclusion:** operable patients with no signs of mediastinal involvement may benefit from presurgical staging with EBUS-TBNA
Electromagnetic navigation

Electromagnetic location board

Locatable guide

Electromagnetic navigation system

Schwarz et al. Respiration 2003;70:516–522
Radiological mapping in coronal, sagittal and axial planes of the CT scan.
Position of the target lesion in a ‘tip-view’ orientation from the sensor probe (right lower quadrant). The cross-hairs indicate the realtime position of the sensor. The tip of the LG is 0.8 mm from the designated target.
Electromagnetic Navigation Diagnostic Bronchoscopy in Peripheral Lung Lesions

92 peripheral lung lesions in 89 subjects
Diagnostic yield of ENB was 67%, independent of lesion size
Total procedure time: mean $\pm$ SD procedure time, 26.9 $\pm$ 6.5 min
Mean navigation error was 9 $\pm$ 6 mm (range, 1 to 31 mm)
Two incidences of pneumothorax for which no intervention was required

**PRO:** yield increases $\pm$ 20% compared to fluoroscopy only

**CON:** Cost of disposable LG prohibitive for SA state sector
US-guided TTNA: Chest wall, Pleura, peripheral lung lesions abutting the chest wall

Diacon AH. Eur Respir J. 2007 Feb;29(2):357-62
US-guided TTNA

Suspicion of Lung Cancer (History, Clinical Signs, CXR)

- Tumor-specific treatment considered?
  - YES
    - Contrasted CT
      - Potentially operable
        - Integrated PET/CT
          - Neg. for M+
          - Neg. for mediast. LNs+
            - Sample PT (FOB +/- EBUS, EUS, TTNA)
              - Neg. N+
                - Mediastinoscopy
                  - Neg. N+
                    - Resection for NSCLC
              - Neoadjuvant Therapy with Reassessment
                - FvG, CTB 4.09
  - NO
    - Inoperable
      - Pos. for M+
        - Pos. for mediast. LNs+
          - Sample PT (FOB +/- EBUS, EUS)
          - Sample LNs +/- PT (FOB +/- EBUS, EUS)
            - Neg. N+
              - Neoadjuvant Therapy with Reassessment
            - N2
              - Palliative Oncologic Therapy
            - N3
              - Best Supportive Care
      - Rule out other pathology

Neg. for mediast. LNs+

Sample most accessible site
**Did you know?**

Lung cancer: the importance of seeing a respiratory physician

3855 lung cancer pat. (Scottish Cancer Reg. 1995)

<table>
<thead>
<tr>
<th></th>
<th>Respiratory Physician (RP)</th>
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<tbody>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Survival 1y %</td>
<td>24.4</td>
</tr>
<tr>
<td>3y %</td>
<td>8.1</td>
</tr>
<tr>
<td>Multidiscipl.</td>
<td>67.5</td>
</tr>
<tr>
<td>Approach%</td>
<td></td>
</tr>
<tr>
<td>Rel. hazard ratio of death if no RP:</td>
<td>1.44</td>
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