Minimally invasive techniques for the Diagnosis and Staging of Lung Cancer

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Conflicts of interest

- None that are economically induced
- I don’t sit on any “boards”
- I don’t own medical related stocks
- I got paid to talk by Boston Sci
- I don’t even like Olympus
- I am biased in some views but not due to person economic factors
Objectives

- What is IP
- Discuss what EBUS is
- Review applications
- Review scientific literature
- Discuss what ENB is
- Review applications
- Review scientific literature
What is IP?

- **Diagnostic bronchoscopy**: bronchialveolar lavage (BAL), fine needle aspirate (FNA), transbronchial lung biopsy (TBBx), endobronchial biopsy, Autoflourescence bronchoscopy (AFB)
- **Advanced endobronchial diagnostics**: endobronchial ultrasound, electromagnetic navigation bronchoscopy (ENB)
- **Treatment of endobronchial cancer**: photodynamic therapy (PDT), APC, cryotherapy, electrocautery and stenting
- **Relief of benign obstruction**: balloon dilation, argon plasma coagulator (APC), electrocautery, cryotherapy, RF/thermal ablation
- **Pleural diagnostics**: thoracentesis, pleural biopsy, pleuroscopy
- **Pleural treatments**: pig tail and large bore chest tube placement with ultrasound or fluoroscopic guidance, pleurodesis, pleurx tunneled chest tube placement
- **Treatment of hemoptosis**: Argon Plasma Coagulator (APC), balloon dilation
- **Advanced airway management**: fiber optic intubation, percutaneous tracheostomy, Endotracheal “scoop” catheter placement, treatment of benign stenosis, tracheal injury and malacia
Interventional Pulmonology

- Minimally invasive diagnostic and therapeutic interventions for:
  - lung
  - mediastinal
  - pleural diseases
Lung cancer diagnosis

- Traditional
  - Bronchialveolar lavage (BAL)
  - Transbronchial needle aspirate (TBNA)
  - Transbronchial lung biopsy (TBBx)
  - Endobronchial biopsy (EBBx)

- Advanced
  - New technologies
EBUS

Endobronchial Ultrasound
EBUS

- Types
  - Radial - balloon
  - Linear - real time biopsy
Utility

- Mediastinal staging
- Centralized mass/nodule biopsy
- Assess airway invasion
- Fiducial marker placement
New advent in staging
LN staging

Lymph node Metastasis in small Peripheral Adenocarcinoma of the Lung
- 157 patients
- 27 N1 - 5 Yr survival 30% +/- 22%
- 130 N0 - 5 Yr survival 91% +/- 6%
ACCP Guidelines 2003

- CT chest (20): pooled sensitivity 0.57 (95% CI, 0.49 to 0.66), specificity was 0.82 (95% CI, 0.77 to 0.86).
- PET (18): pooled sensitivity 0.84 (95% CI, 0.78 to 0.89), specificity was 0.89 (95% CI, 0.83 to 0.93).
- EUS-NA (5): pooled sensitivity was 0.88 (95% CI, 0.82 to 0.93), specificity was 0.91 (95% CI, 0.77 to 0.97).
- TBNA (not EBUS)(12): overall sensitivity 0.76 (95% CI, 0.72 to 0.79), specificity was 0.96 (95% CI, 0.91 to 1.00).
- TTNA (5): overall sensitivity of TTNA was 0.91 (95% CI, 0.74 to 0.97)
- Mediastinoscopy (14): overall sensitivity was 0.81 (95% CI, 0.76 to 0.85) The overall NPV was 91% (range, 58 to 97%)
Table 3—Cervical Mediastinoscopy in Lung Cancer Patients*

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Patients, No.</th>
<th>Patient Type</th>
<th>Feasibility, %</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>FP, %</th>
<th>FN, %</th>
<th>Prevalence, %</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Hammond et al10/1999</td>
<td>1,369</td>
<td>oI–III</td>
<td>100</td>
<td>85</td>
<td>100</td>
<td>0</td>
<td>8</td>
<td>36</td>
<td>8% SCLC</td>
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<td>1,259</td>
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<td>De Leyn et al8/1996</td>
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<td>oI–III</td>
<td>76</td>
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<td>13</td>
<td>39</td>
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<td>Lardinois13/2003</td>
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<td>8</td>
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<td>VMS</td>
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<td>Brion et al7/1985</td>
<td>153</td>
<td>oI–III</td>
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<td>100</td>
<td>0</td>
<td>15</td>
<td>35</td>
<td>5% SCLC</td>
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<td>Jolly et al8/1991</td>
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<td>oI–III</td>
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<td>0</td>
<td>9</td>
<td>54</td>
<td>7% SCLC</td>
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<td>Ratto et al8/1990</td>
<td>123</td>
<td>oI–III</td>
<td>88</td>
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<td>6</td>
<td>33</td>
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<tr>
<td>Ebner et al8/1999</td>
<td>116</td>
<td>oI–III</td>
<td>81</td>
<td>100</td>
<td>0</td>
<td>18</td>
<td>50</td>
<td>11% SCLC</td>
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<tr>
<td>Godeo et al8/1997</td>
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<td>oI–III</td>
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<td>9</td>
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<td>Deneffe et al8/1983</td>
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<td>Aaby et al8/1995</td>
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<td>Pagé et al8/1987</td>
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<td>18% SCLC</td>
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<td>Dillemans et al8/1994</td>
<td>331</td>
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<td>Kimura14/2003</td>
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<td>85</td>
<td>100</td>
<td>0</td>
<td>8</td>
<td>36</td>
<td>VMS</td>
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<tr>
<td>Roca et al8/1991</td>
<td>74</td>
<td>oII–III</td>
<td>81</td>
<td>100</td>
<td>0</td>
<td>16</td>
<td>50</td>
<td>3% SCLC</td>
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<tr>
<td>Venissac6/2003</td>
<td>154</td>
<td>oIII</td>
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<td>100</td>
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<td>6</td>
<td>71</td>
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<td>oII–III</td>
<td>82</td>
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<td>0</td>
<td>13</td>
<td>49</td>
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<tr>
<td>Choi et al15/2003</td>
<td>291</td>
<td>oI</td>
<td>44</td>
<td>100</td>
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<td>9</td>
<td>15</td>
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<tr>
<td>Cussé8/2002</td>
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<td>cNO</td>
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<tr>
<td>Total</td>
<td>6,505</td>
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<td>78</td>
<td>100</td>
<td>0</td>
<td>11</td>
<td>39</td>
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</table>

*VMS = videomediastinoscopy; ? = not defined.
†Excluded peripheral oI; included central, oII, and oIII.
Table 6—EBUS-NA of the Mediastinum in Lung Cancer Patients*

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Patients, No.</th>
<th>Patient Type</th>
<th>Technique</th>
<th>Feasibility, %</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>FP, %</th>
<th>FN, %</th>
<th>Prevalence, %</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herth et al²⁵/2006</td>
<td>502</td>
<td>oI-II</td>
<td>RT-US bronch (22 ga)</td>
<td>94</td>
<td>100</td>
<td>0 (89)</td>
<td>98</td>
<td></td>
<td>25% SCLC</td>
<td></td>
</tr>
<tr>
<td>Yasufuku et al¹⁰¹/2005</td>
<td>108</td>
<td>oI-II</td>
<td>RT-US bronch (22 ga)</td>
<td>100</td>
<td>95</td>
<td>100</td>
<td>0</td>
<td>11</td>
<td>69</td>
<td>16% SCLC</td>
</tr>
<tr>
<td>Yasufuku et al¹⁰²/2004</td>
<td>70</td>
<td>oI-II</td>
<td>RT-US bronch (22 ga)</td>
<td>100</td>
<td>95</td>
<td>100</td>
<td>0</td>
<td>10</td>
<td>67</td>
<td>14% SCLC, 22% other cancers</td>
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<tr>
<td>Vielmann et al¹⁰³/2005; ‡</td>
<td>31</td>
<td>oI-II</td>
<td>RT-US bronch (22 ga)</td>
<td>100</td>
<td>85</td>
<td>100</td>
<td>0</td>
<td>28</td>
<td>65</td>
<td>6% of SCLC</td>
</tr>
<tr>
<td>Rintoul et al¹¹²/2005</td>
<td>20</td>
<td>oI-II</td>
<td>RT-US bronch (22 ga)</td>
<td>100</td>
<td>79</td>
<td>100</td>
<td>0</td>
<td>30</td>
<td>70</td>
<td>14% SCLC</td>
</tr>
<tr>
<td>Kanoh et al¹⁰⁴/2005</td>
<td>24</td>
<td>oII-II</td>
<td>Catheter (19 ga)</td>
<td>100</td>
<td>90</td>
<td>100</td>
<td>0</td>
<td>37</td>
<td>81</td>
<td>30% SCLC</td>
</tr>
<tr>
<td>Plat et al¹⁰⁵/2006</td>
<td>33</td>
<td>oII-II</td>
<td>Catheter (histo needle)</td>
<td>93</td>
<td>100</td>
<td>0</td>
<td>25</td>
<td></td>
<td>82</td>
<td>19% SCLC</td>
</tr>
<tr>
<td>Herth et al¹⁰⁷/2006</td>
<td>100</td>
<td>oI</td>
<td>RT-US bronch 22 ga</td>
<td>94</td>
<td>100</td>
<td>0</td>
<td>1</td>
<td></td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>

Summary: 918 patients, 90% feasibility, 100% specificity, 20% prevalence.

*RT-US bronch = real-time ultrasound bronchoscope. See Tables 3 and 5 for abbreviations not used in the text.
†Excluded from calculations because NPV is relatively less reliable with a prevalence of > 90%.
‡Both EBUS-NA and EUS-NA were performed in each patient. Only values from EBUS-NA were used in calculating the summary statistics.
Staging dilemma

ACCP Guidelines 2007

- Radial EBUS TBNA
  - (8 studies 918pts)
  - 90% Sensitivity
  - 100% Specificity

- Highest sensitivity for any “invasive” staging technique
EBUS

- Ultrasound guides FNA (EBUS-TBNA)
- Increases bronchoscopic yield of lymph node TBNA
- Diagnosis and staging in same procedure
  - Conscious sedation
  - Avoids more invasive procedures
  - Cost savings
EBUS
EBUS yield

Conventional vs endobronchial ultrasound-guided transbronchial needle aspiration: a randomized trial.

- Herth F; Becker HD; Ernst A
- **Objective**: Determine yield of EBUS-TBNA vs. conventional-TBNA in a RCT
- **Methods**: Consecutive patients randomized to EBUS-guided vs. conventional TBNA. A + result was lymphocytes or a specific abnormality on cytology.
- **Results**: 200 pts examined. 50% underwent EBUS-guided TBNA rather than conventional TBNA. In subcarinal LN, the yield of conventional TBNA was 74% vs. 86% in the EBUS group (p=not significant). In other LN stations, the yields were 58% and 84%, respectively (p < 0.001).
- **Conclusion**: EBUS guidance significantly increases the yield of TBNA in all stations except in the subcarinal region. It should be considered to be a routine adjunct to TBNA.
Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically normal mediastinum

- F. J. F. Herth et al
- Eur Respir J 2006; 28:910-914
- **Objective:** Determine accuracy of EBUS-TBNA in LN’s 1 cm dia
- **Methods:** NSCLC patients with CT scans showing no LN > 1cm in the mediastinum underwent EBUS-TBNA. All patients underwent subsequent surgical staging. Diagnoses based on aspiration results compared with surgical results.
- **Results:** In 100 patients 119 lymph nodes ranging 5–10 mm in size were detected and sampled. Malignancy detected in 19 patients but missed in two; all diagnoses confirmed by surgical findings. The sensitivity of EBUS-TBNA was 92.3%, specificity was 100%, and the negative predictive value was 96.3%. No complications occurred.
- Operable patients with no signs of mediastinal involvement on CT may benefit from pre-surgical EBUS-TBNA and staging. 1 in 6 would avoid surgery.
EBUS and EUS

Transesophageal Endoscopic Ultrasound-Guided Fine-Needle Aspiration (EUS-FNA) and Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration (EBUS-TBNA) Biopsy: a Combined Approach in the Evaluation of Mediastinal Lesions

- **Objective:** Combine EUS and EBUS mediastinal staging
- **Methods:** 119 lesions sampled
- **Results:** Accuracy of EUS-FNA and EBUS-TBNA, in combination, for the diagnosis of mediastinal cancer was 100 % (95 % CI, 83 - 100 %)
Minimally Invasive Endoscopic Staging of Suspected Lung Cancer

- MB Wallace JAMA. 2008;299(5):540-546. 1
- **Objective:** Compared TBNA, EBUS-TBNA, EUS-FNA
- **Methods:** 138 patients, 42 (30%) had malignant lymph nodes.
- **Results:** EBUS-FNA was more sensitive than TBNA, detecting 29 (69%) vs 15 (36%) malignant lymph nodes ($P = .003$).
- Combination of EUS-FNA and EBUS-FNA (EUS plus EBUS) had higher estimated sensitivity (93% [39/42]; 95% confidence interval, 81%-99%) and negative predictive value (97% [96/99]; 95% confidence interval, 91%-99%) compared with either method alone.
## Table 3. Estimated Sensitivities and Negative Predictive Values (NPVs) for Separate and Paired Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Sensitivity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBNA</td>
<td>15/42 (36)</td>
<td>96/123 (78)</td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>29/42 (69)</td>
<td>96/109 (88)</td>
</tr>
<tr>
<td>EBUS-FNA</td>
<td>29/42 (69)</td>
<td>96/109 (88)</td>
</tr>
<tr>
<td>EUS-FNA + TBNA</td>
<td>33/42 (79)</td>
<td>96/105 (91)</td>
</tr>
<tr>
<td>EBUS-FNA + TBNA</td>
<td>32/42 (76)</td>
<td>96/106 (91)</td>
</tr>
<tr>
<td>EUS-FNA + EBUS-FNA</td>
<td>39/42 (93)</td>
<td>96/99 (97)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; EBUS-FNA, endobronchial ultrasound-guided fine-needle aspiration; EUS-FNA, transesophageal endoscopic ultrasound-guided fine-needle aspiration; TBNA, transbronchial needle aspiration.

aFor sensitivity, fraction indicates No. of positive cases detected by test/No. positive by diagnostic standard. For NPV, fraction indicates No. of true-negative results/No. of true-negative plus false-negative results by the procedure.

A combined approach of endobronchial and endoscopic ultrasound-guided needle aspiration in the radiologically normal mediastinum in non-small-cell lung cancer staging — a prospective trial

- **Artur Szlubowski et al.** Eur J Cardiothorac Surg 2010;37:1175-1179
- **Methods:** Radiologically normal mediastinum in 120 Patients with NSCLC: 318 mediastinal nodes biopsied (158 EBUS, 160 EUS)
- **Results:** CUS revealed metastatic involvement in 19/120 patients (16%) 99 patients with negative CUS had subsequent mediastinoscopy
  - Metastatic nodes diagnosed in 9 patients (8%) in 11 stations
- **Sensitivity** 68% (95% confidence interval 48–84), specificity 98% (95% CI: 92–100), total accuracy 91% (95% CI: 86–96), positive predictive value (PPV) 91% (95% CI: 70–99) and negative predictive value (NPV) 91% (95% CI: 83–96) of CUS-NA for normal mediastinum
Cost effective

Endobronchial ultrasound guided transbronchial needle aspiration of mediastinal lymph nodes for lung cancer staging: a projected cost analysis

- Objects: Assess cost analysis of EBUS
- Results: The national tariff for mediastinoscopy was £2157, and actual unit based cost was £2000.
- Cost of fiberoptic bronchoscopy was £575. The projected unit based cost to the hospital for EBUS-TBNA was £484.
- “We calculated that the introduction of an EBUS-TBNA service would save the local NHS economy £32 631 per year (including capital costs).”
Accurate mediastinal staging is crucial to the selection of the optimal therapy for patients without distant metastases. Imaging studies are not sufficiently reliable in many situations, making invasive staging tests an important part of appropriate staging. Many different invasive staging tests, which should be viewed as complementary to one another because they are applicable to particular nodal stations and patient groups, are available. It is helpful to separate patients into different groups based on the extent of mediastinal involvement by CT scan and whether the primary tumor is central or peripheral. In general, needle techniques are most useful in patients with enlarged mediastinal nodes, while mediastinoscopy remains the "gold standard" in patients with normal-sized nodes.
Centralized lesions

EBUS-TBNA for the diagnosis of central parenchymal lung lesions not visible at routine bronchoscopy

- KG Tournoy et al. Lung Cancer 63(1) 2009:45-49
- *Objects:* evaluate yield of EBUS-TBNA for diagnosing centrally located lesions after a non-diagnostic conventional bronchoscopy
- *Results:* 60 patients, 82% had a prior (non-diagnostic) flexible bronchoscopy. EBUS-TBNA confirmed lung cancer in 46 (77%). A final reference pathology diagnosis was available in 59 (98%)
- The sensitivity of EBUS-TBNA for diagnosing lung cancer was 82% (95% confidence intervals (CI) 69–91%) with a negative predictive value of 23% (95%CI 5–53%).
Centralized lesion
Correlation between endobronchial ultrasonography (EBUS) images and histologic findings in normal and tumor-invaded bronchial wall

- **B Masayuki et al. Lung Cancer** 35(1) 2002:65-71

- **Objects**: examine the ability of endobronchial ultrasonography (EBUS) to image the bronchial wall structure in order to assess the depth of bronchial tumor invasion.

- **Methods**: 61 patients who underwent lobectomy, pneumonectomy or forceps biopsy were included. 20mHz radial EBUS
  - 21 patients bronchoscopically visible bronchial malignant tumors
  - 40 patients ultrasonography was performed on the resected specimens.

- **Results**: A good correlation was observed between the EBUS-determined cartilage thickness and the actual histologic measurement, as measured with vernier calipers.
Therapeutic use

Real-time endobronchial ultrasound guided implantation of radiotherapy monitoring devices

- F R McGuire et al JoB 2007;14(1)
- EBUS guided fiducial marker placement
  - Targeted radiotherapy
  - Can do mediastinal and endolesional markers
Fiducial placement in mediastinum
ENB

Electromagnetic Navigational Bronchoscopy
Traditional diagnosis

- Central lesions: Bronchoscopy 70:30 rule
Traditional diagnosis

- Peripheral lesions
  - CT guided percutaneous biopsy
    - Pooled sensitivity was 86% in a meta-analysis including 48 studies.
    - High complication rate, 25% pooled incidence of pneumothorax
  - Thoracotomy
    - 40-50% of thoracotomies find benign lesions
  - New technology
New Application of Technology

- ENB using *superDimension/Bronchus System*
  - a novel method to increase endoscopic diagnostic yield of peripheral and mediastinal lung lesions.
superDimension

- ENB
  - Uses GPS technology
  - Mat under patient
  - Probe to map and match airway
  - 3D CT reconstruction and virtual bronchoscopy
Benefits

- Increases yield of bronchoscopy
- Allows biopsy in compromised patients
- Lower risk of pneumothorax compared to percutaneous needle biopsy
  \(<5\% \text{ vs. } 25\%\>
- Allows brachytherapy and fiducial placement
Electromagnetic navigation diagnostic bronchoscopy: a prospective study.

- Gildea TR; Mazzone PJ; Karnak D; Meziane M; Mehta AC

**OBJECTIVES:** A prospective, open label, single-center, pilot study

**METHODS:** 60 subjects enrolled. The mean peripheral lesions size was 22.8 +/- 12.6 mm.

**RESULTS:** The yield/procedure was 74% and 100% for peripheral lesions and LN’s, respectively. A diagnosis was obtained in 80.3% of bronchoscopic procedures. Pneumothorax occurred in two subjects.

**CONCLUSION:** Electromagnetic navigation bronchoscopy is a safe method for sampling peripheral and mediastinal lesions with high diagnostic yield independent of lesion size and location.
Radiotherapy Monitoring Device Insertion into Peripheral Lung Cancers: A Therapeutic Utility of Electromagnetic Navigational Bronchoscopy

- F R McGuire et al.; 200714(3) 173-76 JoB
- Coiled Fiducials can be placed into lesions for stereotactic radiation therapy
Cases
Case 1

- 66yo Male with COPD
- Found to have a RLL nodule and R hilar LAD
- CTPT – positive R perihilar region
- Bronch - negative
- CT guided - negative, pnuemothorax

Wanted to get an answer
Case 1
Case 1

- Dx- Squamous cell
- RLL nodule positive
- R hilar LN negative
- Being evaluated for resection
Case 2

- 78yo Male with HTN
- Recent dx of Hyponatremia- SIADH and ITP
- Started on prednisone and IVIG

- Complains of hoarseness
- CT neck nonrevealing, Laryngoscopy revealed R VC paralysis

- Afebrile, 15# wt loss
- Found to have RML and RUL nodules with some cavitation
- Recent ppd negative
Cases
EBUS
Case 2

- Dx- Suppurative inflammation
- AFB Positive
Case 3

- 48yo Female
- CP
- Cardiac CT
- Mediastinal and hilar LAD
Case 3

Hilum

Paratracheal
Case 3

- Dx- Granulomatous Lymphadenitis
- Sarcoidosis
- Treated with steroids and LAD resolved
Thank you

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