Novel Approaches to Lung Cancer and Airway Diseases: an Interventional Pulmonary Perspective

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Disclosures

- None
Objectives

- Introduce Interventional Pulmonary Medicine
- Update on approach to commonly encountered pulmonary diseases
- Demystify a variety of procedures
Thoracentesis
Chest Tubes
Flexible Bronchoscopy
- Cultures
- Blind Biopsies (+/- Fluoro)
# Interventional Pulmonary Procedures

## Bronchoscopy
- Flexible/Rigid
  - Endobronchial Ultrasound
    - Convex
    - Radial
  - Laser
  - Cryotherapy
- Navigational Bronchoscopy
- Bronchoplasty
- Stents
- Bronchial Thermoplasty
- Bronchopleural Fistula
- Endoscopic Lung Volume Reduction
- Autofluorescence
- Narrow Band Imaging

## Pleural Disease
- Thoracoscopy
  - Pleural Biopsy
  - Pleurodesis
  - Tunneled Pleural Catheters
- Others
  - Bedside Percutaneous Tracheostomy
  - Bedside PEG tube placement
Interventional Pulmonary Procedures

BRONCHOSCOPY
- Flexible/Rigid
  - Endobronchial Ultrasound
    - Convex
    - Radial
  - Laser
  - Cryotherapy
- Navigational Bronchoscopy
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PLEURAL DISEASE
- Thoracoscopy
  - Pleural Biopsy
  - Pleurodesis
  - Tunneled Pleural Catheters
- Others
  - Percutaneous Tracheostomy
  - PEG tube placement
Case # 1

- 59 year old male with a 35 pack year history of tobacco use and COPD presents to his internist with cough and fevers.
- A Chest X-ray is obtained and shows an infiltrate and a possible 2cm nodule
- He is treated for an exacerbation, and a chest CT is obtained.
53,454 randomized to CXR or low dose chest CT
- 55-74 years old
- 30 pack years (quit <15 years)

20% mortality reduction
Nodules in Era of CT Screening

- 96% false positive
- Number needed to screen – 1 in 320
- Positive test = non-calcified nodule >4mm
8.9 million NLST eligible Americans
94 million current and former smokers
Validation of risk calculators
www.brocku.ca/lung-cancer-risk-calculator

Table 3. Outcomes of Three Rounds of Annual Low-Dose CT Screening, According to Risk Quintile.*

<table>
<thead>
<tr>
<th>Quintile of 5-Year Risk of Lung-Cancer Death</th>
<th>Participants</th>
<th>Lung-Cancer Cases</th>
<th>Lung-Cancer Deaths</th>
<th>Positive Screening Results</th>
<th>Number of False Positives per Prevented Lung-Cancer Death†</th>
<th>Number Needed to Screen‡‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. (%)</td>
<td>Total No.</td>
<td>Stage I† no. (%)</td>
<td>Total No. Prevented† no. (%)</td>
<td>Total No.</td>
<td>False Positive†§ no. (%)</td>
</tr>
<tr>
<td>All quintiles</td>
<td>26,604 (100)</td>
<td>1083</td>
<td>530 (48.9)</td>
<td>354</td>
<td>88 (24.9)</td>
<td>10,151</td>
</tr>
<tr>
<td>Quintile 1: 0.15–0.55%</td>
<td>5,276 (19.8)</td>
<td>71</td>
<td>40 (56.3)</td>
<td>20</td>
<td>1 (5.0)</td>
<td>1,699</td>
</tr>
<tr>
<td>Quintile 2: 0.56–0.84%</td>
<td>5,310 (20.0)</td>
<td>105</td>
<td>59 (56.2)</td>
<td>35</td>
<td>10 (28.6)</td>
<td>1,879</td>
</tr>
<tr>
<td>Quintile 3: 0.85–1.23%</td>
<td>5,396 (20.3)</td>
<td>182</td>
<td>84 (46.2)</td>
<td>45</td>
<td>13 (28.9)</td>
<td>2,024</td>
</tr>
<tr>
<td>Quintile 4: 1.24–2.00%</td>
<td>5,314 (20.0)</td>
<td>263</td>
<td>132 (50.2)</td>
<td>73</td>
<td>31 (42.5)</td>
<td>2,123</td>
</tr>
<tr>
<td>Quintile 5: &gt;2.00%</td>
<td>5,308 (20.0)</td>
<td>462</td>
<td>215 (46.5)</td>
<td>181</td>
<td>33 (18.2)</td>
<td>2,426</td>
</tr>
</tbody>
</table>

NEJM 2013; 369: 245-254
National Comprehensive Cancer Network (NCCN)
- Recommends screening per NLST guidelines
- OR age >50, 20 pack year, add’l risk factor
  - Fam Hx, COPD, occupational, other cancer

American College of Chest Physicians (ACCP)

American Society for Clinical Oncology

American Thoracic Society
- Grade 2B – “in centers similar to NLST participants”
USPSTF – December 2013 – Grade B Recommendation –
The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults ages 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

“SEC. 2713. COVERAGE OF PREVENTIVE HEALTH SERVICES.
“(a) IN GENERAL. — A group health plan and a health insurance issuer offering group or individual health insurance coverage shall, at a minimum provide coverage for and shall not impose any cost sharing requirements for — “(1) evidence-based items or services that have in effect a rating of ‘A’ or ‘B’ in the current recommendations of the United States Preventive Services Task Force;
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Loyola Nodule Screening Clinic

- Will follow NCCN guidelines (NLST criteria)
- Multidisciplinary – Oncology, Pulmonary, Radiology, Surgery
- EPIC Order
  - Nurse Coordinator
    - Screen Patient
    - Will Order CT if appropriate
- CT will be free via grant support
- Coming Soon
# Low Dose CT Radiation Info

<table>
<thead>
<tr>
<th>For this procedure:</th>
<th>* Your approximate effective radiation dose is:</th>
<th>Comparable to natural background radiation for:</th>
<th>** Additional lifetime risk of fatal cancer from examination:</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHEST:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT, full body</td>
<td>10-12 mSv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background radiation</td>
<td>3 mSv/yr (6 mSv at high altitude)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequent flyers</td>
<td>1-7 mSv/yr</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Radiological Society of North America
Peripheral Nodule

Options

- Surveillance/Imaging
- Surgery
- CT guided bx
- Bronchoscopy
- Guided bronchoscopy
Peripheral Nodule

PATIENT PREFERENCES

4.4.1.1. In the individual with a solid, indeterminate nodule that measures > 8 mm in diameter, we recommend that clinicians discuss the risks and benefits of alternative management strategies and elicit patient preferences for management (Grade 1C).

SURGICAL MANAGEMENT

4.5.1.3. In the individual with a solid, indeterminate nodule that shows clear evidence of malignant growth on serial imaging, we recommend nonsurgical biopsy and/or surgical resection unless specifically contraindicated (Grade 1C).

4.6.3.1.1. In the individual with a solid, indeterminate nodule that measures > 8 mm in diameter, we suggest surgical diagnosis in the following circumstances (Grade 2C):

- When the clinical probability of malignancy is high (> 65%)
- When the nodule is intensely hypermetabolic by PET or markedly positive by another functional imaging test
- When nonsurgical biopsy is suspicious for malignancy
- When a fully informed patient prefers undergoing a definitive diagnostic procedure.

CHEST 2013; 143(5)(Suppl):e93S–e120S
Peripheral Nodule

Options

- Surveillance/Imaging
- Surgery
- CT guided bx
- Bronchoscopy
- Guided bronchoscopy
CT Guided Biopsy

Population-Based Risk for Complications After Transthoracic Needle Lung Biopsy of a Pulmonary Nodule: An Analysis of Discharge Records

Table 2. Clinical Outcomes in Patients Who Had Computed Tomography–Guided Lung Biopsy, by Presence of Complication and Timing of Biopsy

- Yield 90%
- Pneumothorax rate 15-25%
Conventional Bronchoscopy
Mean nodule size 1.4cm
+ role for central lesions
**Solitary Pulmonary Nodule**

### Table 2—Bronchoscopy Yield by Size of the Lesions*

<table>
<thead>
<tr>
<th>Size</th>
<th>Malignant</th>
<th>Benign</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2 cm</td>
<td>7/30 (23)</td>
<td>8/20 (40)</td>
<td>15/50 (30)</td>
</tr>
<tr>
<td>2.1 to 2.5 cm</td>
<td>7/18 (39)</td>
<td>1/2 (50)</td>
<td>8/20 (40)</td>
</tr>
<tr>
<td>2.6 to 4 cm</td>
<td>43/69 (62)</td>
<td>48/58 (83)</td>
<td>91/127 (71)</td>
</tr>
<tr>
<td>&gt; 4 cm</td>
<td>48/58 (83)</td>
<td>1/2 (50)</td>
<td>49/60 (82)</td>
</tr>
<tr>
<td>All lesions</td>
<td>106/177 (60)</td>
<td>9/26 (35)</td>
<td>115/183 (63)</td>
</tr>
</tbody>
</table>

(CHEST 2000; 117:1049-1054)
Guided Bronchoscopy

Radial Probe – Endobronchial Ultrasound
Guided Bronchoscopy

Bronchoscopic Access
iLogic™ catheters (LG and EWC) go through the mouth or nose to steer through the bronchial tree to lymph nodes and distal lesions

Patient Sensor Triplets (satellites)
Placed on the patient and are "tracking sensors" to show LG position and account for patient movement

Locatable Guide (LG)
360° (8-way) steerability for navigation to the lesion and lymph nodes

Extended Working Channel (EWC)
Lock the EWC in place at the lesion for insertion of endoscopic tools for biopsy and other catheters

Location Board
Creates an electromagnetic field
Guided Bronchoscopy
Guided Bronchoscopy
PTX rate 1.5%. 0.6% required intervention
Pneumothorax rate 1.5%. 0.6% required intervention
Combined Approach

Multimodality Bronchoscopic Diagnosis of Peripheral Lung Lesions
A Randomized Controlled Trial  Am J Respir Crit Care Med Vol 176. pp 36–41, 2007

- 120 patients
- EBUS vs EMN vs Combined
### TABLE 5. DIAGNOSTIC YIELDS BY SIZE, LOCATION, AND DISEASE TYPE, AND PNEUMOTHORAX RATE

<table>
<thead>
<tr>
<th></th>
<th>EBUS, n (%)</th>
<th>ENB, n (%)</th>
<th>EBUS and ENB, n (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall diagnostic yield</strong></td>
<td>27/39 (69)</td>
<td>23/39 (59)</td>
<td>35/40 (88)</td>
<td>0.02*</td>
</tr>
<tr>
<td><strong>Yield by lesion size</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 20 mm</td>
<td>7/9 (78)</td>
<td>3/4 (75)</td>
<td>9/10 (90)</td>
<td>0.02*</td>
</tr>
<tr>
<td>20–30 mm</td>
<td>16/23 (70)</td>
<td>11/22 (50)</td>
<td>21/24 (88)</td>
<td></td>
</tr>
<tr>
<td>&gt; 30 mm</td>
<td>4/7 (57)</td>
<td>9/13 (69)</td>
<td>5/6 (83)</td>
<td></td>
</tr>
<tr>
<td><strong>Yield by lobar location</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.01*</td>
</tr>
<tr>
<td>Bilateral upper lobes</td>
<td>16/27 (59)</td>
<td>17/22 (77)</td>
<td>17/20 (85)</td>
<td></td>
</tr>
<tr>
<td>Right middle lobe</td>
<td>3/3 (100)</td>
<td>2/3 (67)</td>
<td>2/2 (100)</td>
<td></td>
</tr>
<tr>
<td>Bilateral lower lobes</td>
<td>8/9 (89)</td>
<td>4/11 (29)</td>
<td>16/18 (89)</td>
<td></td>
</tr>
<tr>
<td><strong>Yield for malignant disease</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.009*</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>23/32 (72)</td>
<td>16/29 (55)</td>
<td>28/31 (90)</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>7/7 (100)</td>
<td>10/10 (100)</td>
<td>9/9 (100)</td>
<td></td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>23/23 (100)</td>
<td>16/16 (100)</td>
<td>28/28 (100)</td>
<td></td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>7/16 (44)</td>
<td>10/23 (44)</td>
<td>9/12 (75)</td>
<td></td>
</tr>
<tr>
<td><strong>Yield for benign disease</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.16</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>4/7 (57)</td>
<td>7/10 (70)</td>
<td>7/9 (78)</td>
<td>0.79</td>
</tr>
<tr>
<td>Specificity</td>
<td>32/32 (100)</td>
<td>29/29 (100)</td>
<td>31/31 (100)</td>
<td></td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>4/4 (100)</td>
<td>7/7 (100)</td>
<td>7/7 (100)</td>
<td></td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>32/35 (91)</td>
<td>29/32 (91)</td>
<td>31/33 (94)</td>
<td></td>
</tr>
<tr>
<td>Pneumothorax rate</td>
<td>2/39 (5)</td>
<td>2/39 (5)</td>
<td>3/40 (8)</td>
<td>0.99</td>
</tr>
</tbody>
</table>
3.3.2.1. In patients suspected of having lung cancer, who have a peripheral lung nodule, and a tissue diagnosis is required due to uncertainty of diagnosis or poor surgical candidacy, radial EBUS is recommended as an adjunct imaging modality (Grade 1C).

3.4.2.1. In patients with peripheral lung lesions difficult to reach with conventional bronchoscopy, electromagnetic navigation guidance is recommended if the equipment and the expertise are available (Grade 1C).

CHEST 2013; 143(5)(Suppl):e142S–e165S
Navigational System

- Upfront and catheter expense
- Extra CT often required
- Extra time (planning, procedure time)
- Subset of patients without lymphadenopathy
- “Prisoner of the airway”
- “Bronchus sign”
Trans-Parenchymal Nodule Access
Case #2

- 59 year old male with a 15 pack year history of tobacco use and COPD presents to his internist with cough.
- A Chest X-ray is obtained and shows a nodule.
- A Chest CT is obtained with a suspicious nodule, prompting a PET scan.
Case # 2

• Non-diagnostic CT guided biopsy
  • Wrong procedure
  • Complication
Cancer + Sarcoid
2.3.2. In patients suspected of having lung cancer, who have extensive infiltration of the mediastinum based on radiographic studies and no evidence of extrathoracic metastatic disease (negative PET scan), it is recommended that the diagnosis of lung cancer be established by the least invasive and safest method (bronchoscopy with TBNA, endobronchial ultrasound-guided needle aspiration [EBUS-NA], endoscopic ultrasound-guided needle aspiration [EUS-NA], transthoracic needle aspiration [TTNA], or mediastinoscopy) (Grade 1C).
Convex EBUS

Convex Probe EBUS (CP-EBUS)

Outer Diameter: 6.9mm
Scanning Range: 90 degrees
Instrument Channel: 2.8mm
Optics: 30 degrees forward oblique

Department of Thoracic Surgery
Chiba Univ. Graduate School of Medicine
Stage the mediastinum

Cervical Mediastinoscopy
Endobronchial Ultrasound
Esophageal Ultrasound
102 potentially operable patients
- Comparison CT, PET, EBUS-TBNA
- Surgical histology was the gold standard
# Convex EBUS

## Table 4—Characteristics of CT, PET, and EBUS-TBNA in the Correct Prediction of Mediastinal Lymph Node Staging*

<table>
<thead>
<tr>
<th>Tests</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>76.9</td>
<td>55.3</td>
<td>37.0</td>
<td>87.5</td>
<td>60.8</td>
</tr>
<tr>
<td>PET</td>
<td>80.0</td>
<td>70.1</td>
<td>46.5</td>
<td>91.5</td>
<td>72.5</td>
</tr>
<tr>
<td>EBUS-TBNA</td>
<td>92.3</td>
<td>100</td>
<td>100</td>
<td>97.4</td>
<td>98.0</td>
</tr>
</tbody>
</table>

*Data are presented as %. When the results of the three modalities were analyzed using $\chi^2$ tests describing the correct prediction of the lymph node status, the outcome was highly significant ($p < 0.00001$).

Chest 2006; 130:710-718.
EBUS vs Mediastinoscopy

A prospective controlled trial of endobronchial ultrasound-guided transbronchial needle aspiration compared with mediastinoscopy for mediastinal lymph node staging of lung cancer

(J Thorac Cardiovasc Surg 2011;142:1393-400)

<table>
<thead>
<tr>
<th></th>
<th>EBUS</th>
<th>Mediastinoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>81%</td>
<td>79%</td>
</tr>
<tr>
<td>NPV</td>
<td>91%</td>
<td>90%</td>
</tr>
<tr>
<td>Diagnostic Acc</td>
<td>93%</td>
<td>93%</td>
</tr>
</tbody>
</table>
Cost Effectiveness

Cost-Benefit of Minimally Invasive Staging of Non-small Cell Lung Cancer
A Decision Tree Sensitivity Analysis
(J Thorac Oncol. 2010;5: 1564–1570)

• EBUS-TBNA - A$ 2961 (A$ 2477 - A$ 3848)
• Mediastinoscopy - A$ 8859 (A$ 6876 - A$ 12756)
Convex EBUS

- Staging and diagnosis simultaneously
- Additional evaluation of the mediastinum
# Convex EBUS

**PROS**
- Stage and Diagnose
- Real time sampling
- Sample more sites
- Non-surgical/No preop testing
- Avoid general anesthesia
- Ability to resample
- Cheaper

**CONS**
- Training
- Upfront Cost
- Lymphoma?
  - Low yield for Hodgkins
Case # 3

- 48 y/o female with a history of metastatic cervical cancer, presents with worsening dyspnea over the last few weeks
- Previously living independently, is now short of breath getting dressed and has a refractory cough.
- Looks well, but has diminished breath sounds on the right. Oxygen saturation 84% on room air on arrival
Endoscopic View

Right Main Stem Central Airway Obstruction
Conventional Therapy

- Flexible Bronchoscopy
  - Unable to control bleeding
  - Unable to adequately remove tissue
  - Time

- Chemo/Radiation
  - Can take weeks to work
  - May be contraindicated if infected i.e. postobstructive pneumonia
  - Limited dosing
Rigid Bronchoscopy

- Traditionally thought of as tool for foreign body retrieval
  - Larger tools for debridement and stent placement
  - Control of the airway
  - Safer
  - Faster

- Lost art – ‘rediscovered’ by Interventional Pulmonary
Palliative benefits

Therapeutic Rigid Bronchoscopy Allows Level of Care Changes in Patients With Acute Respiratory Failure From Central Airways Obstruction (Chest 1997;112;202-206)

- 62% transferred to lower level of care
- Survival 2 days – 363 days

Table 2—Patient Disposition Before and After Therapeutic Rigid Bronchoscopy

<table>
<thead>
<tr>
<th></th>
<th>Patients With Cancer (n=14)</th>
<th>Patients With Benign Disease (n=18)</th>
<th>Total No. of Patients (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before rigid bronchoscopy</td>
<td>8</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>Patients without indwelling airway</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>After rigid bronchoscopy</td>
<td>8*</td>
<td>1</td>
<td>9*</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>9*</td>
<td>1</td>
<td>10*</td>
</tr>
<tr>
<td>Patients without indwelling airway</td>
<td>4</td>
<td>9</td>
<td>13</td>
</tr>
</tbody>
</table>
Survey – 11 patients
All expressed immediate relief
Survival 0.5 to 34 weeks
Provide significant benefits
- Immediate symptom relief
- Reduces intensity of care
- Palliative
- May allow for additional treatment
Case # 4

- 35 y/o female has been on high dose inhaled corticosteroids and long acting beta agonists for years.
- She is adherent to inhalers, requires oral steroids every 1-2 years and has never been hospitalized.
- She heard an ad about bronchial thermoplasty on the radio and wants to know if she should have the procedure done.
Bronchial Thermoplasty

National Asthma Education and Prevention Program Guidelines (modified)
Bronchial Thermoplasty

- Novel treatment for patients with severe asthma – symptomatic
- Endoscopic delivery of thermal energy (65 C)
  - Reduce airway smooth muscle
  - Reduce capacity for bronchoconstriction
  - Reduce frequency and severity of exacerbations
Bronchial Thermoplasty

- 3 separate treatments – 3 weeks apart
- 50mg prednisone peri-procedure
Bronchial Thermoplasty

- Disrupts airway smooth muscle – diminished cytokines – reduced inflammation
- Denature smooth muscle proteins
AIR 2 Trial

Effectiveness and Safety of Bronchial Thermoplasty in the Treatment of Severe Asthma
A Multicenter, Randomized, Double-Blind, Sham-Controlled Clinical Trial

- 297 patients – ICS > 1000ug + LABA; +/- no more than 10mg prednisone
- FEV1 > 60%
- EXCLUDED –
  - >3 hospitalizations or infections in last 12 months
  - >4 pulses of steroids in last 12 months
  - Chronic sinus disease
  - Uncontrolled GERD
8.4% of those treated required hospitalization periprocedure
Effects maintained 5 years later

~10% reduction in ICS dose, LABA dose, or all meds
Conclusions

- BT appears safe
- Magnitude of benefits?
- Careful patient selection
- Await post market data for more severe patients
- FDA approved – covered by Medicare/Medicaid
- Private insurance coverage is a challenge
Guided Bronchoscopy increases yields for peripheral nodules
Endobronchial Ultrasound is an effective tool to evaluate the mediastinum
Rigid bronchoscopy is an important therapeutic and palliative procedure
Bronchial thermoplasty is safe and appropriate in the right patient
Questions?

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