The Importance of Interventional Bronchoscopic Modalities in Lung Cancer

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Disclosures

I have no financial disclosures, affiliations, or conflicts of interest regarding any of the diagnostic modalities or technology discussed in this presentation.
Objectives

1. Recognize the utility of interventional bronchoscopic modalities to diagnose, stage, and treat patients with lung cancer.

2. Define electromagnetic navigational bronchoscopy and endobronchial ultrasound guided trans-bronchial lymph node aspiration.
Lung Cancer

- Epidemiology and Classification
- Screening
- Diagnostic modalities
- Staging/Prognosis
- Optimizing Treatment
Epidemiology

• 228,520 receive this diagnosis annually in the US

• 159,300 die of the disease, more than 50% die within the first year of diagnosis (although this is changing)

• More cancer related deaths annually than Breast, Colon, and Prostate combined

• By far the most common cause of cancer related death in the U.S. and worldwide.

(American Cancer Society 2013)
Epidemiology

Worldwide numbers are worse!

• 1-2 million people die each year--projected to be 10 million by 2030. More than TB, Malaria, HIV

• Full consequences of the tobacco epidemic are yet to come.

• There were 350 million smokers in China as of 2010 (that’s more than the entire US population!)
CLASSIFICATION

NON-SMALL CELL

- Adenocarcinoma and BAC 32%
- Squamous Cell Carcinoma: 29%
- Large Cell: 9%
- Neuroendocrine/Carcinoid
- Unclassified of undifferentiated: 2%

SMALL CELL
MAJOR TYPES

ADENOCARCINOMA

- Most common subtype (used to be squamous)
- 3% are pure BAC (slow growing)
- Occurs in non-smokers
- Hypertrophic pulmonary osteoarthropathies
MAJOR TYPES

SQUAMOUS CELL CARCINOMA

- 2nd most common subtype; mostly smokers
- Tends to occur centrally; tends to bleed
- Hypercalcemia 2/2/ to PTHrp paraneoplastic syndrome
MAJOR TYPES

SMALL CELL LUNG CANCER

• Purely in smokers

• Always considered systemic disease at diagnosis

• Excellent response to chemo initially, always recurs, 5 year mortality >95%.

• Associated with SIADH
EARLY DETECTION AND DIAGNOSTICS: BUILDING A LUNG SCREENING PROGRAM
Program Goals

- Capture Patients
- Improve Diagnostics
- Optimize Treatment
- Accelerate Recovery

Comprehensive Lung Cancer Program
## Capturing Patients


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<thead>
<tr>
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<tbody>
<tr>
<td>All sites</td>
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<td>54</td>
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</tr>
<tr>
<td>Breast (female)</td>
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<td>79</td>
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<tr>
<td>Colon</td>
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<td>59</td>
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<tr>
<td>Pancreas</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Prostate</td>
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<td>76</td>
<td>99</td>
</tr>
<tr>
<td>Rectum</td>
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<td>57</td>
<td>66</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>74</td>
<td>78</td>
<td>81</td>
</tr>
</tbody>
</table>
Funding for Lung Cancer

Trends in 5-year relative survival rates (%) by year of diagnosis, United States 1975 - 2009

- Improved survival...
- Colon
- Prostate
- Lung

NCI Research Funding, by Site

Research $(M) per cancer death

Breast
Colon
Prostate
Lung

Research $ (M) per cancer death
Capturing Patients with Screening

GOALS:

• Detection of Stage I disease
• Target high risk groups
• Decrease disease related mortality
Survival

5-yr Lung Cancer Survival Rate

Stage of Lung Cancer

- I: 67%
- II: 55%
- IIIa: 13%
- IIIb: 6%
- IV: 3%

NLCST Data

20% reduction in lung-cancer specific mortality with LDCT
6.7% reduction in overall mortality with LDCT
### Summary of Current Guidelines

<table>
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<tr>
<th>Primary Criteria</th>
<th>Secondary Criteria</th>
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<tr>
<td>• 55 – 79 years</td>
<td>• Lung cancer survivor</td>
</tr>
<tr>
<td>• ≥ 30 pack-yrs</td>
<td>• ≥ 50 years</td>
</tr>
<tr>
<td></td>
<td>• ≥ 20 pack-yrs</td>
</tr>
<tr>
<td></td>
<td>• At least one other risk factor (not second-hand smoke)</td>
</tr>
<tr>
<td></td>
<td>• Added ≥5% risk of lung CA within 5 years</td>
</tr>
<tr>
<td></td>
<td>• ≥ 50 years</td>
</tr>
<tr>
<td></td>
<td>• ≥ 20 pack-yrs</td>
</tr>
<tr>
<td></td>
<td>• Grade B Recommendation</td>
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</table>

**CMS**

- 55 – 74 years
- ≥ 30 pack-yrs
- Current smoker or quit ≤ 15 yrs
- Asymptomatic

**NCCN**

- 55 – 80 years
- ≥ 30 pack-yrs
- Current smoker or quit ≤ 15 yrs
- Asymptomatic

**U.S. Preventive Services Task Force**

- 55 – 77 years
- ≥ 30 pack-yrs
- Current smoker or quit ≤ 15 yrs
- Asymptomatic

**CMS**

- None
- None
Overdiagnosis: Detection of disease that does not contribute to death

Results in unnecessary treatment, morbidity, cost, worry

Lung Cancer (LDCT) 18%
Breast Cancer (Mammo) 30-54%
Prostate Cancer (PSA) 29-44%
What do we see on CT?
Definition of terms

- **GGO (non-solid):** Nodule with hazy increased lung attenuation which does not obscure underlying bronchovascular markings.

- **Mixed (part-solid):** Nodules containing both ground glass and solid components

- **Solid (soft tissue):** Nodules with attenuation obscuring the bronchovascular structures
Solitary Pulmonary Nodule
Differential Diagnosis

- Granulomas (infectious vs healed) (40%)
- Intrapulmonary lymph nodes
- Benign neoplasms (hamartoma, fibrosis, lipoma) (15%)
- Rheumatoid nodules, other inflammatory nodules
- AVMs
Solitary Pulmonary Nodule Pre-test Probability

• Pre-test probability helps facilitate selection and interpretation of subsequent tests.

• Mayo Clinic Validated model: 6 independent predictors of SPN: Age, Smoking status, History of extrathoracic malignancy, Diameter, Spiculation, Upper lobe Location

• Size: 2-5mm=1%; >2cm=80% chance of malignancy
Solitary Pulmonary Nodule
Pre-test Probability

Low: <5%:
  --Serial follow-up with CT

Intermediate: 5-60%
  --PET, ENB, TTNA, EBUS, Bronch

High: >60%
  --Excisional biopsy
IMPROVING DIAGNOSTICS

- Capture Patients
- Improve Diagnostics
- Optimize Treatment
- Accelerate Recovery

Comprehensive Lung Cancer Program
Improving Diagnostics

• Using chest X-Ray for screening has demonstrated no improvement in mortality or morbidity related to lung cancer.

• Traditional bronchoscopy does not work for diagnosing peripheral lung cancers.
Improving Diagnostics

SuperD

Original Investigation

Diagnostic Yield of Electromagnetic Navigation Bronchoscopy Using a Curved-tip Catheter to Aid in the Diagnosis of Pulmonary Lesions

Sumit Mukherjee, MD, MPH* and Michael Chacey, MD†
Improving Diagnostics: Radial EBUS

A probe that houses an ultrasound transducer which provides 360° radial image of the surrounding structures. Probe is inserted through the working channel of the bronchoscope and advanced to the target lesion.
Improving Diagnostics
Improving Diagnostics: EBUS
Improving Diagnostics: EBUS
LN Staging
Why is EBUS Important?

• Mediastinal staging is the standard of care (NCCN) for most peripheral lesions (unless small) and all central lesions to pathologically assess lymph node involvement.

• PET scan is not enough; near 20% chance of missing microscopic disease.

• IF LN is PET +, must sample node regardless of size to r/o inflammation

• N stage is an important prognostic indicator of overall stage.
# 2017 NSCLC Stage Changes

<table>
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<tr>
<th>T/M</th>
<th>Label</th>
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<th>N2</th>
<th>N3</th>
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<td>IA1</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIB</td>
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<tr>
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<td>T1b &gt;1-2</td>
<td>IA2</td>
<td>IIB</td>
<td>IIIA</td>
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<tr>
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<td>IA3</td>
<td>IIB</td>
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<td>T2</td>
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<td>T2a &gt;3-4</td>
<td>IB</td>
<td>IIB</td>
<td>IIIA</td>
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<td>IIB</td>
<td>IIIA</td>
<td>IIIB</td>
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<tr>
<td>T3</td>
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<td>IIB</td>
<td>IIIA</td>
<td>IIIB</td>
<td>IIIC</td>
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Prognosis Highlights

5-Year Survival (%)

<table>
<thead>
<tr>
<th>Type</th>
<th>IA1</th>
<th>IA2</th>
<th>IA3</th>
<th>IB</th>
<th>IIA</th>
<th>IIB</th>
<th>IIIA</th>
<th>IIIB</th>
<th>IIIC</th>
<th>IVA</th>
<th>IVB</th>
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<tr>
<td>Clinical</td>
<td>92</td>
<td>83</td>
<td>77</td>
<td>68</td>
<td>60</td>
<td>53</td>
<td>36</td>
<td>26</td>
<td>13</td>
<td>10</td>
<td>0</td>
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<tr>
<td>Pathologic</td>
<td>90</td>
<td>85</td>
<td>80</td>
<td>73</td>
<td>65</td>
<td>56</td>
<td>41</td>
<td>24</td>
<td>12</td>
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</tr>
</tbody>
</table>

- Remember that there is significant variability in outcomes by region, and patients in each stage were treated in various ways in various countries.

- Outcomes are substantially better in this database when compared to prior years.

- THIS IS WHY WE SCREEN!!!
OPTIMIZING TREATMENT

- Capture Patients
- Improve Diagnostics
- Optimize Treatment
- Accelerate Recovery

Comprehensive Lung Cancer Program
Optimizing Treatment

Symptom presentation

- Biopsy/ Diagnosis
  - Diagnostic Workup

- Team Discussion
  - Test Ordered

- Tissue Biopsy Test

- ~2 WEEKS POST PROCEDURES RETRIEVE BLOCK FOR TESTING

- Results in 12 days

- Treatment Decision
  - Treatment Begins

- Patient waits for treatment

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5-7 days

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14-21 days

~30 days to treatment

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Current State of Practice
Standard tissue based molecular testing

POTENTIAL LUNG CANCER

IT’S AN EMERGANCY

Life

Treatment

TIME

TISSUE
**EGFR Sensitizing**
- Gefitinib 4
- Erlotinib 4
- Afatinib 4
- Osimertinib 4
- Necitumumab 4
- Rociletinib 3

**ALK**
- Crizotinib 4
- Alectinib 4
- Ceritinib 4
- Lorlatinib 2
- Brigatinib 2

**MET**
- Crizotinib 2
- Cabozantinib 2
- Trastuzumab emtansine 2
- Afatinib 2
- Dacomitinib 2

**HER2**
- Crizotinib 4
- Cabozantinib 2
- Alectinib 2
- Apatinib 2
- Vandetanib 2
- Ponatinib 2
- Lenvatinib 2

**ROS1**
- Crizotinib 4
- Alectinib 2
- NCI-637 3
- NCI-233 3
- NCI-500 3

**BRAF**
- Crizotinib 4
- Alectinib 2
- Apatinib 2
- Vandetanib 2
- Ponatinib 2

**RET**
- Cabozantinib 2
- Alectinib 2
- Apatinib 2
- Vandetanib 2

**PIK3CA**
- Trametinib 2
- Selumetinib 3
- Cobimetinib 1
- LY3023414 2
- PQR 309 1

**NTRK1**
- Entrectinib 2
- LOXO-101 2
- DS-6051b 1

**MEK1**
- Trametinib 2

**Key**
1 - Phase I
2 - Phase II
3 - Phase III
4 - Approved
Mutation Analysis in NSCLC

Timing is important!

Advanced NSCLC

GeneStrat Liquid Biopsy
EGFR, EGFR T790M, KRAS, ALK
ROS1, RET and BRAF

RESULTS IN 72 HOURS

EGFR negative or EGFR Status
Unknown: All Histology

VeriStrat

EGFR, ALK, ROS1, RET or BRAF
Positive:

Targeted Therapy

Mutation Negative:
Proceed to tissue testing
- PDL1
- Biomarkers for trial enrollment

PDL1 Positive

Immunotherapy

PDL1 Negative

VeriStrat Good:
- Plat. Doublets
VeriStrat Poor:
- Clinical Trial or BSC

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Lung Cancer Screening Program

- Medical Oncology
- Thoracic Surgery
- Smoking Cessation
- Referring Physicians
- Chest Radiology
- Radiation Oncology
CONCLUSIONS

• Early detection is key. Low-dose CT screening of high risk patients is now recommended.

• New modalities are available for the diagnosis and staging of lung cancer including electromagnetic navigational bronchoscopy and endobronchial ultrasound

• Proper staging including lymph node sampling is essential in lung cancer.
QUESTIONS?

“"The best way to predict the future is to create it."”

Abraham Lincoln