New Advances in Interventional Pulmonology

Targeted Options for Lung Cancer Treatment 2019

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Conflicts of Interest:

• Nothing to disclose
Objectives:

• Explore current and future directions for interventional pulmonology lung cancer diagnostics and treatments
  – Evolution of peripheral nodule biopsies

• Review 2019 guidelines for malignant pleural effusions (if time permits)
  – Focus on advice relevant to general providers
Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*
Solitary Nodule and Lung Cancer Screening
Location: peripheral vs central?

NELSON trial: 15,822 participants
- 62% in the periphery (outer 1/3rd)
- RUL predominance
Interventional Pulmonology – balance risk/benefit

- A CT-guided approach is often more accurate (95%).
- A surgical approach is often definitive and possibly curative.
- The bronchoscopist's goal should be to approach the yield of these two techniques while providing the lowest morbidity.

**PNEUMOTHORAX**

**MORBIDITY and COST**

- Minimal pneumothorax
- Minimal morbidity
- Least cost
Transthoracic biopsy

Diagnostic yield: 90-95%

Complications:
- Pneumothorax 10-17%: ~ 7% require chest tube
- Hemorrhage 1%

No significant difference in yield between lesions < 2cm and > 2cm

De Margerie-Mellon Diag & Interv Imaging 2016
Wiener Annals of Int Med 2011
Manhire BTS guidelines Thorax 2003
Benefits of Bronchoscopic Approach

- Lower risk of pneumothorax (~1%)
- Opportunity to stage simultaneously (EBUS lymph node sampling)
- Potential for direct lesion visualization
- Better able to assess non-malignant causes for nodules (e.g. infection)
### Conventional Bronchoscopic Methods: Location matters

<table>
<thead>
<tr>
<th></th>
<th>Central Tumors*</th>
<th>Peripheral Tumors</th>
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<tbody>
<tr>
<td><strong>Overall Yield w/ Combined Techniques</strong></td>
<td>88%</td>
<td>78%</td>
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<tr>
<td>Biopsy</td>
<td>74% (Endobronchial tumor)</td>
<td>57% (TBBx)</td>
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<tr>
<td>Washing</td>
<td>48%</td>
<td>43%</td>
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<tr>
<td>Brushing</td>
<td>59%</td>
<td>54%</td>
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For peripheral tumors – yield increased with number of TBBx samples
- 1 sample – 45%
- 6 samples – 70%

* Endobronchial, submucosal tumors and peribronchial with extrinsic compression
Conventional Bronchoscopic Methods: Size matters

- Nodule < 3cm
- Mass > 3cm in largest diameter
- “Conventional” Bronchoscopy
  - BAL/EBBx/TBBx without EBUS/EMN

<table>
<thead>
<tr>
<th>Size</th>
<th>Prevalence of Malignancy</th>
<th>Yield of Conventional TBBx</th>
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<tbody>
<tr>
<td>&lt; 0.5cm</td>
<td>0-1%</td>
<td>~34%</td>
</tr>
<tr>
<td>0.5-1.0 cm</td>
<td>6-28%</td>
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<tr>
<td>1-2 cm</td>
<td>33-64%</td>
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<tr>
<td>&gt; 2 cm</td>
<td>64% - 82%</td>
<td>Up to 63%</td>
</tr>
<tr>
<td>&gt; 3 cm</td>
<td>93-97%</td>
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Advanced Techniques – Getting closer, seeing more

“No, but you’re getting warmer.”
Ultrathin bronchoscopes

- Limitations
  - Smaller working channel
    - Less suction
    - Smaller instruments
  - Less rigidity
  - Poorer image quality
Radial Probe EBUS (RP-EBUS; pEBUS)

- Confirms location of nodule in real time
  - Does not allow “real-time” biopsies
- For detection of lung cancer in peripheral lesions:
  - Pooled sensitivity 73%, specificity 100%
  - Diagnostic yield: 56% < 2cm, 78% > 2cm
Guide Sheath + Radial EBUS

Endobronchial Ultrasound with a Guide Sheath for Biopsy of Peripheral Lesions
Radial EBUS in lesion

Even when lesion is reached, the biopsy is not in “real time”

Diagnostic yield (496 pts):

- Concentric view (within) - 84%
- Eccentric view (adjacent) - 48%
Left Lower Lobe Nodule – How to get there?
Virtual bronchoscopy
Electromagnetic Navigation Bronchoscopy
Meta-Analysis of Navigational Bronchoscopy

- 2015: 17 studies
  - Pooled sensitivity and specificity: 82% and 100%
  - Diagnostic odds ratio: 97%
- 2014: 15 studies, 1033 lung nodules
  - Diagnostic accuracy overall: 73.9%

**Increased yield** → size
- Radial EBUS use
- “bronchus sign”

**Decreased yield** → lower lobe location

Overall pneumothorax rate: Similar to conventional bronchoscopy
Overall Diagnostic Yield with New Technology

- Guide sheath: 73.2%
- Virtual bronchoscopy: 72%
- Radial EBUS: 71.1%
- EMN / ENB: 67%

Pneumothorax rate: 1.6%
Chest tube required: 0.6%

Meta-analysis of 39 studies with over 3000 patients

So What’s New?
Robotic Bronchoscopy

- 3.2mm outer diameter scope, 1.2mm working channel
- 180 degree flex in any direction
- Permits direct continuous visualization of lesions throughout the biopsy procedure
- Deeper reach
  - 9th vs 6th generation airways

- 17 patient feasibility study:
  - “bronchus sign” lesions
  - Direct visualization of biopsy in 14/15
Potential?

- Higher diagnostic yield, approaching that of CT-guided trans-thoracic needle biopsy, with lower rate of complications
- Benefits of bronchoscopy remain – simultaneous diagnosis and staging procedure
- Potential for therapeutic intervention – same-day diagnosis and treatment
  - Radiofrequency ablation
  - Microwave ablation
  - Photodynamic therapy
  - Brachytherapy
  - Vapor ablation
  - Cryoablation
  - Direct injection of chemotherapy
Take Home Points

• As lung cancer screening increases, the need for evaluation of small peripheral lung nodules will rise
• For non-surgical patients, CT-guided needle biopsy has superior diagnostic efficacy but higher risk
• Bronchoscopy can provide simultaneous diagnosis, staging, and possibly therapy in future
• Advances in bronchoscopy permit more accurate tissue acquisition from distal lesions, while maintaining safety profile
• Robotic bronchoscopy is the newest modality
  – Greater peripheral reach
  – Direct visualization of lesions
  – May use other modalities to enhance accuracy (navigation, radial EBUS)
Malignant Pleural Effusions (MPE)

- 2018 – Evidence-based guidelines focusing on management of MPE
  - Management of asymptomatic and symptomatic MPE
  - Use of pleurodesis vs indwelling (tunneled) pleural catheters
  - Management of catheter-associated infection
Asymptomatic MPE – No need to drain

- Porcel et al 2015: Retrospective study of 556 patients with newly diagnosed lung cancer
  - 40% developed pleural effusion
  - ½ of these (112 cases, 20% of total) were too small for sampling or intervention
  - None of these 122 cases went on to require drainage (follow-up 10 +/- 11 months [SD])

- Tremblay et al 2007: Retrospective review of 113 new lung cancer patients
  - 34 had pleural effusion, 14 were asymptomatic
  - 13/14 followed for median 98 days, none needed intervention

In patients with known or suspected MPE who are asymptomatic, we suggested therapeutic pleural interventions not be performed
Will patient get better? – Try large-volume thoracentesis

- A patient’s symptoms may not be due to the effusion
  - Differential includes pre-existing lung disease, tumor impact, PE, pericardial effusion
  - Assess with thoracentesis prior to definitive procedures
  - May learn speed of re-accumulation – up to 60% of patients will require repeat within 9 days of initial drainage\(^1\)

- It is sometimes unclear whether the lung can expand after drainage
  - “nonexpandable lung” occurs in 30% of patients with MPEs, and may be a contraindication for pleurodesis\(^2\)

In patients with symptomatic MPE, if it is uncertain whether the patient’s symptoms are related to the effusion and/or if the lung is expandable, we suggest a large-volume thoracentesis

\(^1\)Ost et al. Chest 2018
Non-expandable lung
Indwelling Pleural Catheter (IPC) associated infection

- Aggregated data from 3 RCTs\(^1\) show IPC-related rates of:
  - Cellulitis = 7.3%
  - Pleural space infection = 4.6%
- 6 observational studies and 1 nested case series:
  - 41/57 patients (72%) managed without removing the IPC
  - No data to suggest superiority/inferiority of catheter continuation vs removal

- The problem for which the catheter was placed (MPE) still remains
- Initial treatment of pleural infection is...chest tube placement and drainage.
- Pleurodesis may result after infection!

**In patients with IPC-associated infection, treating through the infection without catheter removal is usually adequate.**

\(^1\) Feller-Kopman et al. AJRRCM 2018.
Take Home Points for MPE

• If there is no diagnostic question and the MPE is asymptomatic, drainage is not required
• To determine whether the MPE is symptomatic or whether the lung is re-expandable, perform large-volume thoracentesis first
• If fluid rapidly re-accumulates and symptoms re-develop, definitive intervention is advised
• IPC and chemical pleurodesis are both considerations
  – IPC advisable if lung is not re-expanding
• If there is an IPC-associated infection, try to treat through first
References


