Overview of endobronchial ultrasound guided fine needle aspiration (EBUS FNA): benefits and challenges

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EBUS FNA: benefits and challenges

Disclosure of Relevant Financial Relationships
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Dr. Ross A Miller declares he/she has no conflict(s) of interest to disclose.

EBUS FNA: benefits and challenges

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EBUS FNA: benefits and challenges

Lung cancer
- Leading cause of cancer death in the United States and worldwide for men and women
- ~ 85% are non-small cell lung cancers (NSCLC)
  - Adenocarcinoma > Squamous cell carcinoma
- United States: over 200,000 people are diagnosed with lung cancer per year
- Canada: nearly 30,000 people diagnosed per year

So...when a patient presents with a suspected lung cancer, how are they evaluated?

EBUS FNA: benefits and challenges

PRESENTATION TITLE
EBUS FNA: benefits and challenges

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EBUS FNA: benefits and challenges

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EBUS FNA: benefits and challenges

Please turn off your cell phones.
Suspected lung cancer
• Tissue procurement goals
  • Benign vs malignant
  • Primary lung cancer versus secondary lung cancer
  • Histologic subtype
  • Confirm suspected metastatic disease (staging)
  • Molecular testing

• Ideally, achieve the above in the least number of procedures possible

• So… in the ideal setting, we are obtaining all necessary information while minimizing procedural related risks to the patient

Biopsy target
• Target selection based on multiple factors, tailored to the patient
  • Maximize information, minimize the number of procedures, and minimize potential harm to the patient
  • “Primum non nocere” First, do no harm

• Factors taken into consideration
  • History and physical exam, laboratory findings
  • What type of procedure can the patient tolerate?
  • Chest CT, possible PET or other imaging studies (if done…)

• Goal: Determine the clinical stage

Biopsy target
• Suspected distant metastatic disease → stage IV
  • In this setting, the metastatic lesion is often sampled
    • Ease of targeting, less patient risk
    • Patient is not a surgical candidate

So…EBUS procedures are likely not used much in this setting

Biopsy target
• Suspected stage IA (T1aN0M0 or T1bN0M0), peripheral lesion
  • No suspected nodal/distant metastasis
  • These patients are considered surgical candidates

• Surgical resection of the lung lesion with lymph node sampling
  • Nodals: peribronchial/hilar

No nodal involvement → no need for further therapy (Stage 1A)

If there is nodal involvement (stage II, N1 disease) → adjuvant chemotherapy

So…EBUS procedures may potentially be used to look for nodal disease
Biopsy target

- Suspected Nodal involvement
  - Specifically, suspected stage IIIA/B: N2 and N3 disease
  - N2: ipsilateral, mediastinal node or subcarinal node
  - N3: contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, supraclavicular
- Biopsy target: often the lymph node
- Confirms presence of disease
- The distinction between Stage IIIA (N2 disease) and IIIB (N3) disease is important
  - IIIA: may be eligible for chemo followed by surgery
  - IIIB: not surgical candidates
- As such, may want to target more than one node if clinically suspicious

EBUS procedures are often requested

EBUS FNA: benefits and challenges

Endobronchial ultrasound (EBUS) fine needle aspiration (FNA) and biopsy

- Combines bronchoscopy with ultrasound, FNA or biopsy can be obtained
- Indications
  - Staging or re-staging non-small cell lung carcinoma
  - Obtaining tissue for diagnosis on large central lung tumors
  - Workup of lymphadenopathy
  - Diagnosis or “ruling out” sarcoidosis, lymphoma, or metastatic disease (non-lung)
  - Sampling mediastinal masses
  - Usually superior and anterior mediastinal tumors
  - Before EBUS: cervical mediastinoscopy used to stage

EBUS FNA: Advantages

- Ability to sample lung and mediastinal lesions
  - Less invasive than mediastinoscopy/surgery
  - More cost effective than surgical mediastinoscopy
- Generally safe, complications are relatively uncommon
  - Agitation, cough, bleed
  - Some probes used for peripheral nodules, bleeding/pneumothorax
  - Infection/fistula formation is rare
- Good Sensitivity and Specificity!

EBUS FNA: benefits and challenges

Historical Overview

- 1949: Transbronchial needle aspiration described - rigid bronchoscope (Schieppati)
- 1983: TBNA used through a flexible bronchoscope (Wang and colleagues)
- Used to stage lung cancer
- 1992: ultrasound applied to bronchoscopy
- 1999: EBUS bronchoscope became commercially available
- Improvements and advances made since

EBUS FNA: benefits and challenges

Cervical Mediastinoscopy

EBUS FNA: benefits and challenges
PRESENTATION TITLE

EUS and EBUS

“medical mediastinoscopy”

EBUS
- Potential to sample
  - 2R and 2L
  - 4R and 4L
  - 7
  - 11
  - Sometimes 12

EBUS
- Potential to sample
  - 8
  - 9
  - Left adrenal

EBUS FNA: Challenges
- Limited or no diagnostic material obtained
  - May require a second staging procedure (mediastinoscopy)
- Requires an endoscopist with expertise
  - Proper training programs are a necessity!
  - No current method in place to assess competency/technical skills
- Some targets cannot be assessed due to anatomic location
  - Combined EUS and EBUS are sometimes used, “medical mediastinoscopy”
    - Complementary procedures with better sensitivity

EBUS FNA and rapid on-site evaluation (ROSE)

Advantages
- “Real time” evaluation of procured material
  - Evaluates if lesion tissue is being sampled and allows the physician performing the FNA to make additional passes if needed
  - Improves accuracy of staging
  - Fewer passes, superior adequacy rates
  - Improved patient care, less repeat procedures
- The performance of FNA is dependent on specimen adequacy and sampling
  - Up to one-third are nondiagnostic when ROSE is not utilized
  - Some studies suggest ROSE does not make a difference in diagnostic yield
  - Task force guidelines have suggested
    - ROSE is only effective in reducing additional procedures
    - No statistically significant differences in # of aspirations, diagnostic yield, time, or complications
    - One expert panel recommended tissue sampling with or without ROSE in patients undergoing EBUS-TBNA for diagnostic evaluation of lung cancer (Grade 1C)

EBUS FNA and rapid on-site evaluation (ROSE)

Advantages
- Allows preliminary information to be relayed
- Specimen triage for ancillary studies
  - Flow cytometry, Microbiology studies, Molecular testing, Cell block preparations
  - Potential to give guidance on how to improve yield/technique
    - More on this...
  - Sampling can be stopped when diagnostic material is obtained
    - Opposed to doing a set number of passes
- Builds relationship between pathologist and endoscopist: better patient care

Pulmonary pathology consensus paper (soon to be submitted)

Rapid on-site evaluation of endobronchial ultrasound guided transbronchial needle aspirations (EBUS-TBNA) for the diagnosis of lung cancer

Lead author: Jain Deepali

EBUS FNA: benefits and challenges
Clinically suspect stage IIIA disease
4L lymphadenopathy
N2: ipsilateral mediastinal node

So.. we want to obtain tissue
- least number of procedures possible
- obtain sufficient material for histologic subtyping and molecular studies

EBUS FNA, Station 4L, lymph node

Initial Pass

Subsequent passes

Papanicolaou stain

EBUS FNA, Station 4L, lymph node

Cell block

Molecular Diagnostics Result:
- KRAS mutation detected
- EGFR wildtype
- BRAF wildtype
- NABK analysis
- PD-L1 gene analysis by FISH: negative
- A. non-small cell lung cancer (NSCLC) (PD-L1) was observed
- B. positive (PD-L1, PD-L1, PD-L1, PD-L1) was observed
- C. positive (PD-L1, PD-L1, PD-L1, PD-L1) was observed
- D. positive (PD-L1, PD-L1, PD-L1, PD-L1) was observed
- E. TMB gene analysis by FISH: negative
- F. negative (PD-L1, PD-L1, PD-L1, PD-L1) was observed
- G. negative (PD-L1, PD-L1, PD-L1, PD-L1) was observed
- H. negative (PD-L1, PD-L1, PD-L1, PD-L1) was observed
- I. negative (PD-L1, PD-L1, PD-L1, PD-L1) was observed
- J. negative (PD-L1, PD-L1, PD-L1, PD-L1) was observed

EBUS FNA, Station 4L, lymph node
Another example
60 M with mediastinal lymphadenopathy

Pass #1

Recommendations?

Papanicolaou stain

Cell block

ROSE: Potential to give guidance on how to improve yield/technique

- The performing physician has to be receptive...
- FNA technique
- "aspiration" biopsy is a misnomer!
- Needle into lesion
- Visualized via ultrasound (convex probe)
- Distal end grooved: more hyperechoic on US
- Stylet moved in and out to dislodge bronchial wall contaminant
- Stylet removed
- Movement: "aspiration" (pull back on syringe)
- Make excursions!
- 2-3 per second, long amplitude
- Negative pressure without proper needle movement is insufficient for tissue collection, needle movement "cuts the tissue", negative pressure "debris into needle"
- Limit dwell time 5-10 seconds maximum, shorter (2-5 seconds) for nodes/vascular lesions
- Release vacuum
- Now pull needle out of lesion

Additional sources for slide:
3) Murgu S, Davoudi M, Dolt H. EBUS Step by Step video available on YouTube
4) Personal experience and training

Dwell time too long
"the needle is in the lesion….
but that does not mean the lesion is inside the needle

- Technique issues
- Bronchial wall material pushed into the target and then taken up by the needle when excursions are made
  - Repeat FNA
  - Move stylet 'back and forth'

Challenges of ROSE

- Need a pathologist experienced with ROSE
- Time consuming
- Average amount of time per site sampled: 12-22 minutes
  - Often more than one site sampled
    - We found the average pathologist adequacy assessment time was ~38 min
    - Range 2-142 min
- Current Medicare compensation rates are insufficient to cover Pathology costs (adequacy assessment CPT code 88172)

Challenges of ROSE

- One study suggests training interventional pulmonologists or using cytotechnologists for ROSE
  - Over 90% concordance with cytopathologist
- Caution: this would really be an adequacy assessment only
  - Limited literature on this
- Telecytology can be used

Challenges of ROSE

- Although pathology costs exceed reimbursement, the overall cost of EBUS is far less than mediastinoscopy
- However (and more important than cost) ROSE has value
  - Improves procedural outcomes
  - Reduces the need for repeat procedures
EBUS FNA: benefits and challenges

• Reduces need for additional procedures
• Specimen Triage
• Adequacy assessment
• Improves diagnostic yield
• Builds relationship between pathologist and endoscopist
• Overall: improved patient care

When feasible, ROSE should be provided – plenty of literature supporting the use of ROSE
Better overall EBUS-FNA performance

Take home messages about ROSE

Advantages:
• Adequacy assessment
• Specimen Triage
• Reduces need for additional procedures
• Improves diagnostic yield
• Builds relationship between pathologist and endoscopist
• Overall: improved patient care

Disadvantages:
• Requires experienced pathologist
• Time and cost

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No claims can be processed after that date!

After September 30, 2017 you will NOT be able to obtain any CME or SAMs credits for attending this meeting.

Thank you
Supplemental slides

EBUS FNA: benefits and challenges

7th Ed
M1a: Separate tumor nodule(s) in a contralateral lobe tumor with pleural nodules or malignant pleural (or pericardial) effusion

M1b: Distant metastasis

7th Ed | 8th Ed | 7th | 8th
---|---|---|---
M1a | M1a | IV > T1a | M1a
M1b single lesion | M1b | IV > T1a | M1b
M1b multiple lesions | M1b | IV > T1b | M1c

Needle types
- 21, 22, 25 gauge
- Stainless steel and nitinol
- ProCore needle
  - Pilot study did not show ProCore needle to add value
  - Medical literature: recommends use of either a 21 or 22 gauge needle
  - Needle size is usually determined by the operator based on the location (station) of the LN, vascularity of the node, and the type of specimen processing (cytology versus histology)

Radial probe vs Convex probe
- Radial probe (RP-EBUS) image
  - Gives a 360 degree image of the airway and surrounding structures
- Convex probe
  - Image parallel to shaft of bronchoscope
  - Used when performing TBNA
Molecular testing

• ~80% of lung cancers diagnosed at advanced stage, a portion diagnosed by cytology or small biopsy
• Material obtained from EBUS procedures may be (and often is) the only material available for molecular testing
• Molecular testing dependent on multiple factors
  • Overall cellularity and tumor fraction
  • Analytic sensitivity of the molecular testing platform
• Material suitable for molecular testing in >90% of samples


EBUS FNA: benefits and challenges

Study by Yarmus et al:
• EGFR and KRAS sequencing
• ALK FISH
• 95% of specimens were satisfactory