EBUS-FNAB: HOW TO OPTIMIZE YOUR CYTOLOGY SAMPLES, LHSC EXPERIENCE

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Objectives

• Brief overview of EBUS-FNA
• Strategies to optimize cytology samples
• Role of adequacy assessment (ROSE)
• Terminology, diagnostic challenges
• Lessons learned from LHSC
  • Where we were and where we are now…
Lung Cancer: Facts

- Lung cancer - leading cause of cancer death (male and female)
- In Canada 21,700 new cases and 18,900 deaths/yr
- Mediastinal nodal staging is a key modality in management
Mediastinal Nodal Staging

- Imaging modalities – without tissue sampling
  - CT
  - PET
  - Integrated PET-CT

- Modern methods - with tissue sampling *to improve staging accuracy*

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediastinoscopy</td>
<td>81</td>
<td>100</td>
</tr>
<tr>
<td>EBUS-FNA</td>
<td>89</td>
<td>100</td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>89</td>
<td>100</td>
</tr>
<tr>
<td>EBUS+EUS FNA</td>
<td>91</td>
<td>100</td>
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</tbody>
</table>

ENM – electromagnetic navigational biopsy (latest, very expensive)
Nodal Stations/Procedures
EBUS – FNA Procedure
EBUS – FNA Procedure

Fewer passes.
More information.
EBUS FNA: Advantages

- Minimally invasive procedure, cost effective
- Safe in experienced hands (major complication 0.15%)
- Excellent sensitivity, specificity, PPV, NPV
- Can sample lung and mediastinal nodes
  - Lung ca including post chemo staging
  - Metastatic cancer, melanoma, lymphoma (76% sensitivity)
  - Granulomatous disease
    - Sarcoid (86% sensitivity)
    - Infection
EBUS Procedure at LHSC

- Started by Dr. Dave McCormack, respirologist (2010)
- Now 4 thoracic surgeons, 2 respirologists
  - EBUS (6) EUS (2)
- 250 cases (2014)
- Standardized cytology practice
The value of ROSE for EBUS-FNA is well recognized. A recent metanalysis showed that with ROSE, sensitivity is 88% (80% without)
DEBATE IS AROUND WHETHER ROSE SHOULD BE PERFORMED FOR EVERY PROCEDURE OR ONLY SELECTIVELY?

LHSC – ROSE DONE ON ALL CASES (8 CTS)

Mean # of passes = 4 (2-9)
Usually on 1-2 samples
ROSE time: 25-55 minutes
Dr. McCormack, LHSC (300 cases)

For the diagnosis of malignancy our results show:

- Sensitivity: 95%
- Specificity: 100%
- Positive predictive value: 100%
- Negative predictive value: 93%

We are very happy with these results. Thanks to you and your staff for being so supportive and helpful.

Dr. D. McCormack
It is well recognized that ...

- Success of EBUS-FNA depends on the combined skill and competency of the pulmonologists, cytotechnologists and cytopathologists – Total health care team
Competent FNA Cytotechnologists (ROSE)

- Milestone approach to training, team teaching
- Pathologists feedback and teaching are essential
- Cooperation from clinicians and support from administration are essential

Ref: ASC bulletin commentary on ROSE position statement
March 2015
Communication During ROSE

- ADEQUATE
  - Specimen sample is adequate
  - Specimen sample is adequate but please obtain more material for
    - Cell block
    - FCM
    - Microbiology

- NOT ADEQUATE
  - Specimen sample is NOT adequate
  - There is nothing here
  - I need more, low cellularity
  - We need to go back

Cytotechns cannot provide a diagnosis
EBUS FNA: OPTIMIZING SAMPLES AND REPORTING

Sample processing
Adequacy
Terminology
Ancillary tests
Olympus Needle

Pass 1 & Pass 3 (as needed)

Place some material on a slide. Make 2 smears per pass. Air dry one slide for Diff-Quik stain and Rapid On-site Evaluation. Spray fix second slide for Pap stain and final evaluation.

FNAB + Needle Rinses

Pass 1&3 Needle Rinses

Place all samples in CytoLyt solution

Pass 2, 4 and Beyond

For suspected lymphoma, place a sample in Flow medium

Cytology Lab

Thin Prep Slide

Cell Block
Assess cellularity and select the appropriate block for immuno and molecular tests.
Adequacy for Nodal Sampling

Criteria not well established
• 40 lymphocytes per HPF in cellular areas of slide or pigmented macrophage clusters - Alsharif et al

Our criteria
Abundant lymphocytes >100/LPF in 5 fields or abundant dust laden macrophage clusters and scant respiratory cells
Adenocarcinoma

Small Cell Carcinoma
Cell Block, Granuloma, likely Sarcoid
LUNG CANCER REPORTING TERMINOLOGY
Diagnostic Terminology in Cytology

- NE carcinomas
  - Small cell carcinoma
  - Possible LCNEC (immuno +)
  - NSCLC with NE morphology
- Adenocarcinoma
- Squamous cell carcinoma
- NSCLC favor squamous cell ca (immuno +)
- NSCLC favour adenocarcinoma (immuno+)
- NSCLC NOS (use only rarely, immuno inconclusive)

Ref: Travis: Arch Pathol Lab Med. 2013;137:668–684
IASLC/ATS/ERS Classification—for details
Non small cell carcinoma

<table>
<thead>
<tr>
<th>Marker</th>
<th>Adenocarcinoma</th>
<th>Squamous cell ca</th>
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</thead>
<tbody>
<tr>
<td>TTF1 *</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>CK5/6, p63* or p40</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Napsin</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Mucin*</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Molecular EGFR or ALK</td>
<td>+</td>
<td>–</td>
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</tbody>
</table>

- *Used at LHSC
- * mucin may or may not be used, PASD or mucicarmine
- If mixed immuno pattern call NSCLC NOS, may represent adenosquamous ca

Arch Pathol Lab Med. 2013;137:668–684
Adenocarcinoma

Squamous Cell Ca

TTF-1 Negative
P63 Positive
Malignant Cells in Cell Block
Semi-quantitation by CTs

• Scant <10 cells
• Low 10-50 cells
• Medium 50-100 cells
• High >100 cells

• This would allow oncologists and pathologists to order additional molecular tests (e.g. EGFR) on appropriate samples, i.e. cell blocks with medium and high cellularity are preferred.
EBUS-EUS Interpretation Challenges

- Cellular contaminants (en route)
  - Tracheobronchial columnar cells
  - Seromucinous glands, cartilage
  - Esophageal squamous cells - EUS

- Atypical/dysplastic epithelium
- Reserve cell hyperplasia
- Mucinous metaplasia
- Epithelioid histiocytes
- Crushed lymphocytes

Can be challenging during ROSE
MOLECULAR TESTING: EGFR, ALK

Priority for NSCLC stage 4 cancers
Optimize sample size
Adenocarcinoma – LHSC 2010…still learning

Cell block: low cellularity
10-50 cells
Adenocarcinoma, LHSC - 2014

Cell block cellularity:
>100 cells (high)
TTF-1 +, p63 –ve
Adequate sample for EGFR and ALK testing

DO NOT TRIM SIGN
Metastatic Melanoma

73 F, EBUS - FNA Subcarinal (#7) Node

HMB 45
EBUS FNA Practice - Summary

- Multidisciplinary team work, emphasize team teaching
- Use standardized procedures & diagnostic terminology
- Multidisciplinary Tissue Management Strategy
  - Perform multiple aspirations (3-6)
  - ROSE only on 2 samples, rest in needle rinse
  - Optimize cell block (Histogel), avoid excessive trimming
  - Minimal immuno for cell typing: p63/p40, TTF-1
  - Preserve as much tissue for NSCLC molecular testing