Lung Biopsy: Technique and Approach in Era of Molecular Pathology

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Objectives

• To understand the role of molecular profiling of lung cancer in personalized medicine
• To review the interventional techniques available for lung tissue acquisition and molecular profiling
• To assess the role of comprehensive RadPath report in assisting the management of patients

Targeting the EGFR and K-Ras pathway

Adapted from Roberts Der. Oncogene 2007, courtesy Dr. Zev Wainberg

B-Raf mutation:

CRC (10%)
Melanoma (70%)
Papillary thyroid cancer (50%)

Ras mutation:

CRC (50%)
Pancreatic cancer (90%)
Papillary thyroid cancer (60%)
NSCLC (30%)

EGFR overexpression:

CRC (27 ± 77%)
Pancreatic cancer (30 ± 50%)
Lung cancer (40 ± 80%)
NSCLC (14 ± 91%)

EGFR mutation:

NSCLC (10%)
Glioblastoma (20%)

MAPK

*Mutated in human cancers

EGFR

Ras

EGFR overexpression:

+ CRC (27-37%)
+ Pancreatic cancer (30-50%)
+ Lung cancer (40-80%)
+ NSCLC (14-91%)

EGFR mutation:

NSCLC (10%)
Glioblastoma (20%)

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Lung Biopsy: Technique and Approach in Era of Molecular Pathology

Fereidoun Abtin M.D.
Thoracic Radiology
Percutaneous lung biopsy and molecular profiling

- Molecular phenotyping
- Drugable Mutations

Objectives

- To understand the role of molecular profiling of lung cancer in personalized medicine
- To review the interventional techniques available for lung tissue acquisition and molecular profiling
  - Diagnosis of lung cancer, metastasis and clinical trial
  - Drugable Mutations
  - Preferred method in era of Molecular profiling

CT-guided Percutaneous Lung biopsy

- Well-established diagnostic method but not often used
  - NLST
  - Sharpe et al. JACR 2013;10:770-773
- Techniques:
  - Fine needle aspiration (FNA)
  - Aspirating cells for cytologic analysis
  - Core needle biopsy
  - Obtaining fragments of tissue for histologic analysis
  - Bronchoscopy and CT directed biopsy
    (Electromagnetic navigated_Superdimension)
  - FNA and tissue

Advantages of core needle biopsy over FNA

- Highly accurate in all practice settings
  - Even without cytology to assess Touchprep (FNA) specimens
  - Lower false negative rate
  - Favored in non-carcinomatous malignancies
    - lymphoma, sarcoma, mesothelioma
  - Superior to FNA in diagnosing benign lesions
  - More tissue available for immunohistochemical tests
  - Help distinguish between primary and metastatic carcinoma
  - If metastatic disease, assist in identifying primary neoplasm

Underutilization of core needle biopsy

- Despite the clear advantages of core needle biopsy over fine needle aspiration, most IR still prefer FNA
  - Fear of Pneumothorax
  - Theoretical increased risk of pneumothorax due to larger-gauge cutting needle employed, compared to smaller aspiration needle
  - Increased risk of lacerating adjacent vessels, which may cause major hemorrhage
  - Vessel laceration also increases the risk of air embolism, a potentially fatal complication

Percutaneous lung biopsy and molecular profiling

- With increasing advances in molecular analysis and targeted therapy, larger amounts of tumor tissue will be needed to identify various somatic mutations
  - Lung CA
  - Metastasis

- Laurent et al. Cardiovasc Intervent Radiol 2000; 23:266
- Li et al. JCO 2013
- Sharpe et al. JACR 2013;10:770-773
- Paez et al. Science 2004; 304:1497-1500
- Li et al. JCO 2013
Migration to Percutaneous Lung biopsy for molecular profiling

- At least 200-400 malignant cells are required to perform biomarker testing. 1
- Trans bronchial biopsy yield ranges from 70% to 40%, with only less than 50% of samples containing tumor cells. 2,3
- CT guided Core-needle: approximately 500 cells per core biopsy. 4

Just EGFR testing is not enough

BATTLE (Biomarker-integrated Approaches of Targeted Therapy for Lung Cancer Elimination) trial

- 170 biopsies w 20 G biopsy needle
- 11 predetermined molecular markers
- At least 2 samples obtained
- 82.9% had sufficient tissue for required biomarker analysis

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Clinical Implications of RadPath report in Lung Ca

- Comprehensive and integrated diagnostic report to assist in management of patients with lung cancer
- Collective findings and interpretations which is responsible for subsequent cancer diagnosis, treatment and outcome.

Clinical Implications of RadPath Program in Lung Ca

- Facilitated single access report through creation of a system that integrates the radiographic, pathologic, and molecular characterization of cancer
- Collaboration of findings and coordination of diagnosis through close communication
- Improved downstream information flow to users
- Review of diagnostic and procedural imaging to ensure sample tissue is true representative of target lesion
- Reassess diagnostic options for Discordant cases
Discordant results

### Final Pathologic Diagnosis:

**Lung Mass, Left Lower Lobe (Needle Core Biopsy):**
- Fibroelastotic scar with markedly atypical alveolar lining cells, highly suspicious for adenocarcinoma-in-situ, nonmucinous, see comment

#### Histologic Grade
- Visceral dehiscence

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**Pathology:** Fibroelastotic scar with markedly atypical alveolar lining cells, highly suspicious for adenocarcinoma-in-situ, nonmucinous

**Radiology:** Invasive carcinoma with lepidic growth

**Conclusions:** Discordant

**Rebiopsy:** Invasive Adenocarcinoma, non-mucinous

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**Clinical Implications of RadPath Program in Lung Ca**

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**Summary**

- Simple diagnosis of lung cancer or lung metastasis is not enough to guide therapy and molecular profiling is needed to detect drugable mutations
- Percutaneous CT guided lung biopsy is a safe modality to obtain tissue
- RadPath report can provide single access comprehensive result and assist in management decisions

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**Thank you**