American Society of Cytopathology
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State of The Art Symposium
Take a Deep Breath!
Current Concepts in Lung Cancer

Radiology, Interventional Radiology, and the Solitary Pulmonary Nodule

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Imaging Evaluation of the SPN
A solitary pulmonary nodule measuring 2 centimeters in diameter is noted on a CT scan of the chest of a patient with no prior history of malignancy. Which of the following features is least likely to be associated with benign pathology?

a. Central nidus of calcification  
b. Focal fat density  
c. Non-solid ("ground glass") appearance  
d. Cavitation associated with thin walls (<4 mm)  
e. Lack of change in size compared to a scan from two years prior
Imaging Evaluation of the SPN

General

- Mainstay of evaluation at the present time CT, occasionally supplemented by PET or detailed evaluation of enhancement characteristics
- Basic rule: obtain old films for comparison if available
- Size not particularly reliable, although in general the larger the lesion (approaching 3 cm) the more likely malignant
Imaging Evaluation of the SPN

Margin

- Irregular/spiculated margins suggestive of malignancy (extension along lymphatics/septae)
- Smooth margins do not as reliably predict benignity (esp. for metastases)
Calcification

- Calcification may occur in up to 13% of primary lung cancers
- Calcification associated more often with certain metastases (malignant carcinoid, chondrosarcoma, osteosarcoma, mucin-secreting tumors)
Imaging Evaluation of the SPN

Calcification

- Certain patterns of calcification in small (< 3 cm) nodules almost always indicate benign pathology
- Central nidus, “popcorn”, laminated, diffuse
- Eccentric calcification warrants followup, if not biopsy
Imaging Evaluation of the SPN

Focal Fat

- When no history of renal cell ca or liposarcoma, fat suggests benign hamartoma or (less likely) lipoma
Imaging Evaluation of the SPN

“Ground-Glass” Appearance

- Approximately 34% of non-solid nodules are malignant
- Risk increases if:
  - Size > 1.5 cm
  - Round
  - Solitary
  - Fails to resolve or decrease in size spontaneously or with treatment in weeks to months
Imaging Evaluation of the SPN

Cavitation

- May occur in both benign and malignant nodules
- Nodules with thick (>16 mm) irregular walls tend to be malignant
- Nodules with thin (<4 mm) walls: 95% benign
Imaging Evaluation of the SPN

Interval Growth

- In general, stability of size over a two year period or longer indicates benign pathology.
- However, be cautious of measurement variability and of pitfall of comparing only to the most recent study (measurement of smaller nodules more inaccurate then larger).
- On occasion, malignant nodules occur with extremely long doubling times (>730 days) that may appear stable over two year followup.
Imaging Evaluation of the SPN

Contrast Enhancement

- Minimal enhancement (<15 HU) strongly suggests benign nodules (99% positive predictive value)
- However, greater degrees of enhancement do not strongly predict malignancy
Evaluation of the SPN

Clinical Features Suggesting Malignancy

- Increasing patient age
- Smoking history
- Current smoker vs. former smoker
- History of cancer

Ost and Fine, Current Opin Pulm Med, 2004
PET (Positron Emission Tomography)
Role in Management of SPN?

• Positive PET in pt. > 60 years, 90% probability of malignancy
• Negative PET <5% malignancy
PET (Positron Emission Tomography)

Role in Management of SPN?

- Decision analysis suggests helpful in patients for whom there is a discordance between appearance of nodule on CT and pretest probability
  - Nodule appears malignant but patient has low risk of cancer
  - Pt has high risk of cancer but nodule appears benign
- May help improve confidence in instituting therapy
15 month followup
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References:

Biopsy of the SPN
Question 2

Which of the following is least likely to improve the diagnostic accuracy of percutaneous image-guided lung biopsy?

a. Use of a core biopsy device as opposed to fine needle aspiration (FNA) in the setting of lymphoma
b. Use of a core biopsy device as opposed to fine needle aspiration (FNA) to obtain a specific benign diagnosis
c. Presence of a cytopathologist on-site for evaluation of biopsy specimens
d. Use of a core biopsy device as opposed to fine needle aspiration (FNA) in the diagnosis of primary lung carcinoma
Biopsy of SPN

Considerations

- Generally indicated for intermediate probability of malignancy based on imaging tests
- High probability but tissue confirmation needed for further therapy (may just consider removal or ablation as well)
- Probability of success lower with smaller nodules, deeper lesions
- Main risks: pneumothorax, bleeding
Biopsy of SPN

**Tools**

- **Basically two choices:**
  - “Fine” needles (but overlap with core devices)—specimen procured using suction or “capillary action”
    - Some fine needles have “cutting” tips
    - 18-25 ga
  - “Core” devices
    - Manual, semiautomated, fully automated
    - Generally larger diameter (18-20 ga)
  - Guiding needles may be used with either
Dx: Metastatic melanoma
Biopsy of SPN

Core vs. FNA: Any difference?

- Lymphoma: FNA lower sensitivity than core (12% vs. 62%)
- Specific benign diagnosis: FNA lower sensitivity than core (16.7% vs. 81.7%)
- Malignant (nonlymphomatous) pulmonary lesions
  - Core biopsy marginally superior for metastatic disease
  - No significant differences in primary lung neoplasms overall
- In one reported study of 156 lesions, core less informative than FNA in 35 (22.4%), mostly those with nonsmall cell lung ca
Biopsy of SPN

On-Site Cytopathology

• Promotes better communication, efficiency and understanding between the two specialties that I believe (anecdotally) best serves patient care
  • At NMH we are involving cytopathology in the physical restructuring of the IR area
• In a clinical study of 55 adults with nonlymphomatous thoracic malignancy, and in a metaanalysis reported in the same study, the presence of a cytopathologist on-site is associated with a significant increase in diagnostic accuracy
Biopsy of SPN

Improved Targeting?

Fluoro-CT: imaging rapidly to provide near-real time visualization of needle being advanced toward lesion

Cost: increased radiation exposure to operator/pt

Various adjunctive needle guides (not especially helpful in my estimation)

Electromagnetic navigation systems—in their infancy but may significantly improve accuracy of needle placement, especially for difficult/small lesions

http://www.traxtal.com
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Interventional Radiology and the SPN: Ablative Techniques
Local Ablative Therapies

- Chemical
  - Ethanol
  - Acetic Acid
  - Hot Saline

- Thermal
  - Radiofrequency ablation
  - Laser
  - Microwave
  - High frequency Focused Ultrasound
  - Cryoablation
Radiofrequency Ablation

Principles

- High frequency alternating current
  - 460-500 kHz
- Local ionic agitation >> frictional heat production >> thermal coagulation of tissues (cell death @ 50°C)
- Electrode *not* the source of heat; rather, it is the tissue near the electrode
Radiofrequency Ablation

Factors Affecting Ablation Success

- Distance from electrode
  - Rapid decrease with distance \((1/r^4)\)
  - Therefore, must guide accurately
    (**guidance methods improving rapidly**)
- Duration (conduction of heat without charring)
- Size of lesion (poorer success esp. > 3 cm)
- Proximity of blood vessels ("heat sink")
RFA: Lung

- Normal lung tissue insulates the tumor
  - Facilitates (theoretically) energy concentration within tumor tissue
- “Ideal” patient
  - Small lesion ($\leq 3$ cm)
  - Solitary lesion
  - Peripheral rather than central
Lung Neoplasias

- Lung/bronchial primaries are the leading cause of cancer death in both men and women (29% of all cancer deaths)
- Five-year survival only 15%
- Surgical therapy often limited by concomitant COPD/CAD or advanced stage of disease
Lung RFA

Technical Considerations

• Strive for 1 cm margin
• Lesions have some tendency to move away from electrode
• Saline infusion?
• Track ablation?
  • Unclear whether beneficial in limiting complications
Lung RFA

Technical Considerations

- General anesthesia vs. MAC vs. moderate sedation?
- Periprocedural antibiotics?
- Post-procedural pain meds
RFA: Lung

Risks/Complications

- **Pneumothorax**
  - Rates requiring chest tube seem to be higher than for lung biopsy (~15-30%)
  - Be prepared to place chest tube (can continue with ablation)
  - Aspiration of air “on the way out” may decrease risk
RFA: Lung
Risks/Complications

• Cerebral microembolism (or macroembolism)?
  • Microbubbles known to be generated in RFA in liver
  • Presumably generated in lung; if so, could travel via pulmonary veins to left heart, then to systemic circulation
  • Air embolism a known complication of TTNB
• Acute cerebral infarction during RFA has been reported*

Jin et al, AJR 2004; 182:990-992
RFA: Lung

Cerebral microembolism

- 20 patients undergoing lung RFA
- Microemboli, believed to represent microbubbles, seen in 3/17 on US/Doppler of carotid artery
- However, no abnormalities seen on MRI
- Concluded that while microemboli may occur, there is a low possibility of a clinical problem
- Incidence may be increased when emission power high

Yamamoto et al, AJR 2004; 183:1785-1789
RFA: Lung

Risks/Complications

- Cough
- Fever
- Dyspnea; RDS
- Chest pain
- Bleeding (larger vessels adjacent seem to protect themselves to some degree)
  - Hemoptysis
  - Hemothorax
- Abscess
- Pleural effusion
RFA: Lung

Followup: CT

- Complete Ablation
  - 40% decrease in size by 12 months (same at 15 months) compared to lesion size immediately post treatment
  - No enhancement

- Partial Ablation
  - Variable degrees of enhancement
  - Mean percentage of ablated lesion size gradually increased after 6 month f/u

Jin et al, AJR 2004; 183:1013-1020
Lung RFA

Results

- 244 patients, 397 tumors
- Primary 19%, metastatic 81%
- Single 58%, unilateral 79%
- Rate of local tumor progression at 2 years significantly better for tumors <2 cm (8.2%) than greater (19.4%)
- 57.5% with no viable tumor at 1 year, 38.8% at two years
- One and two year survival 88.7%/70.3%

de Baere et al, SIR Annual Meeting 2008
Lung Ablation

Future Directions

- Combination with intravascular therapy (e.g. pulmonary artery embolization/chemoembolization)
- Further delineation of factors affecting outcome (cell type, proximity to mediastinum, great vessels, pleural surface)
- More efficient electrodes
- Better guidance
Lung RFA

Conclusions

- RFA successfully treats relatively small pulmonary malignancies
- High rate of complete response for small tumors
- Acceptable morbidity
- May be an alternative or complementary method for patients with non-small cell lung cancer or lung metastases who are not candidates for surgical resection

Lencioni et al, CVIR 2004; 27:581-590
Radiology, IR, and the SPN

**Summary**

- Imaging features essential in decision to perform biopsy
- Percutaneous biopsy generally accurate and safe; importance may grow as therapies “tailored” to specific tumor pathology/genotype
- Ablative therapy: more data needed (RFA and others)
- Expect advances in imaging guidance and ablative techniques