Nuclear Medicine Techniques in Pulmonology
Single most important application of pulmonary scintigraphy: Evaluation of suspected PE

Other indications
– Quantitative analysis of relative lung perfusion before lobectomy/pneumonectomy
– ARDS
# VENTILATION SCINTIGRAPHY

## Radiopharmaceuticals

### Radioactive gases
- $^{133}\text{Xe}$ (most common)
- $^{127}\text{Xe}$
- $^{81}\text{Kr}$
- $^{133}\text{Xe}$: $t_1/2$ – 5.27 days
  - Relative low energy (81-Kev) of its photon
  - Difficult to perform V scan after using Tc$^{99m}$ for Q scan

### Radioaerosols
- DTPA (Tc$^{99m}$ Pentetate)
  - Ideal aerosol size: 0.1-0.5 $\mu m$
  - Localize in alveoli without significant large airway deposition

::: V scan performed first in combined V/Q scan
Protocol for xenon-133 ventilation scintigraphy

- Technique: Radioactive gas
- Patient preparation: None
- Dosage and route of admission
  - Xenon133: 10 to 20 mCi dosage by inhalation
- Procedure
  - Use a wide-field-of-view camera with a parallel hole, all purpose collimator and a 20% window centered at 81 keV
  - The patient is seated with the camera positioned in the posterior view
– First breath: patient exhales fully and is asked to take a maximal inspiration and hold it long enough, if possible, to obtain 100k counts
– Equilibrium: Obtain two sequential 90 sec images while the patient breathes normally
– Washout: Obtain sequential 45 sec posterior image then left and right posterior oblique images and a final posterior image

Sitting position better: full Dm excursion, easier to obtain oblique views

Radio aerosols:
– DTPA Nebulized over several min. [25-75mCi]
– Views obtained [similar to gas studies]
PERFUSION SCINTIGRAPHY

- $\text{Tc}^{99m}$ labelled Human Albumin Microspheres ($\text{Tc}^{99m}$ HAM)
- $\text{Tc}^{99m}$ labelled macroaggregated albumin ($\text{Tc}^{99m}$ MAA)

$\downarrow$

(Commonly used)

- $\text{Tc}^{99m}$ MAA: 10-30μ
- Clearance from lungs
  - Mech. degradation of particles to smaller size → Phagocytosed by RES after passing into systemic circulation
- $T1/2 : 2-3 \text{ hrs}$
- Dose: 60,000-400,000 particles/dose
Patient preparation and precaution

- Right-to-left shunts are a relative contraindication
- Pregnant women: Adjust dosage and observe requirement for a minimum of 60,000 particles
- Pulmonary hypertension or pneumonectomy: Reduce number of particles to 60,000

Dosage and Route of Administration

- Tc-99 MAA: 4 mCi (148 MBq) adult dosage
- Intravenous administration over several respiratory cycles with the patient supine
Procedure

- Use a wide-field of-view gamma camera with a low energy high-resolution or all-purpose collimator and a 20% window centered at 140keV.
- Obtain anterior, posterior, right lateral, left lateral and right and left lateral posterior oblique images (anterior oblique images optimal).
- Obtain 500K to 750K counts/image.
Precaution

- Avoid drawing blood into syringe

↓

Avoid spurious “Hot Spots”

- Agitate syringe before inj.

↓

Avoids setting out and aggregation of particles
APPEARANCE OF NORMAL SCINTIGRAMS

Ventilation Scan
- Wash in image: Homogenous distr. of Xe\textsuperscript{133}
- Equilibrium phase: Homogenous
- Washout phase: Progressive/uniform ↓ in activity from lung

Aerosol Study
- Distr. Similar to gas study
Perfusion Scan

- Normal/healthy individual
  - Homogenous uniform distr.

- Extra pul. Activity:
  - Positive – Rt. – Lt. shunt
  - Radiopharmaceutical contaminant in preparation
PULMONARY EMBOLISM

V/Q Mismatch Concept

- **V/Q match**
  - both scintigrams abnormal
  - defect of equal size

- **V/Q mismatch**
  - Abnormal perfusion in an area of normal ventilation or much larger perfusion abnormality
  - then ventilation defect

Terminology for V/Q scan

- **Segmental defect**
  - Characteristically wedge shaped and pleural based, segmental anatomy of the lung
- Large segmental defect
  - >75% of a lung segment
- Moderate segmental defect
  - 25%-75% of a lung segment
- Small segment defect
  - <25% of a lung segment
- Non-segmental defect
  - Not conform to segmental anatomy, not appear wedge shaped or neither conforms to segmental anatomy nor appears wedge shaped
Causes of Non-segmental Defects

- Tumors
- Pleural effusion
- Trauma
- Hemorrhage
- Bullae
- Cardiomegaly
- Mediastinal and hilar adenopathy
- Atelectasis
- Pneumonia
- Aortic ectasia or aneurysm
<table>
<thead>
<tr>
<th>Revised PIOPED Criteria</th>
<th>PIOPED II V/Q Scan Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High probability (&gt;80%)</strong></td>
<td><strong>High Scan probability</strong></td>
</tr>
<tr>
<td>Two or more large mismatched segmental perfusion defects or the equivalent in moderate or large and moderate mismatched defects</td>
<td>Two or more large mismatched segmental defects or the equivalent in moderate or large and moderate defect</td>
</tr>
<tr>
<td><strong>Intermediate Probability (20%-79%)</strong></td>
<td><strong>Intermediate-indeterminate scan probability</strong></td>
</tr>
<tr>
<td>One moderate to one half large mismatched segmental perfusion defects or the equivalent in moderate segmental perfusion defects</td>
<td>One half to one and one half segmental equivalents, difficult to categorize as high, Multiple opacities with associated perfusion defects</td>
</tr>
<tr>
<td>Single matched V/Q defect with clear chest radiograph</td>
<td></td>
</tr>
<tr>
<td>Difficult to categorize as low or high, or not described as low or high</td>
<td></td>
</tr>
<tr>
<td><strong>Low probability (&lt;19%)</strong></td>
<td><strong>Low Scan Probability</strong></td>
</tr>
<tr>
<td>Non-segmental perfusion defects</td>
<td>A single matched V/Q defect</td>
</tr>
<tr>
<td>Any perfusion defect with a substantially larger chest radiographic abnormality</td>
<td>More than three small segment lesions</td>
</tr>
<tr>
<td>Perfusion defects matched by ventilation abnormality provided that there are a clear chest radiography and some areas of normal perfusion in the lungs</td>
<td>Probable pulmonary embolism mimic: one lung mismatched (without) with absent perfusion, solitary lobar mismatch</td>
</tr>
<tr>
<td>Any number of small perfusion with a normal chest radiograph</td>
<td>Mass or other radiographic lesion causing all mismatch, moderate-sized pleural effusion</td>
</tr>
<tr>
<td>Marked heterogeneous perfusion</td>
<td>Marked heterogeneous perfusion</td>
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</tbody>
</table>
| Normal perfusion Scan | Very low Scan probability  
|-----------------------|---------------------------  
| No perfusion defect    | Non-segmental lesion  
|                       | Perfusion defect smaller than radiographic lesion  
|                       | Two or more V/Q matched defects with regionally normal chest radiograph  
|                       | One to three small segmental perfusion defect  
|                       | Stripe sign present around the perfusion defect  
|                       | Pleural effusion of one third with no perfusion defect  

| Normal                  | Normal perfusion Scan  
|-------------------------|------------------------  
| No perfusion defect     | No perfusion defect    |
High probability scan: Likelihood of PE: 80%
(N) perfusion scan: Likelihood < 5%

Accuracy
- PIOPED trial: Specificity - 97%
  Sensitivity - 41%
- Occurrence of PE in: Low probability – 12%
  Normal study – 4%
D/D of V/Q mismatch

- Acute pulmonary embolism
- Chronic pulmonary embolism
- Other causes of embolism (drug abuse, iatrogenic)
- Bronchogenic carcinoma (other tumors)
- Mediastinal or hilar adenopathy with obstruction of pulmonary artery or veins
- Hypoplasia or aplasia of pulmonary artery
- Swyer-James syndrome
- Post radiation therapy
- Vaculities
  - Chr PE: Most common cause of false +ve interpretation
  - Hilar mass compressing pul artery → mimics PE
V/Q Match Abnormalities

- Chronic obstructive pulmonary disease
- Bronchitis and bronchiectasis
- Blebs and bullae
- Congestive heart failure
- Pulmonary edema
- Pleural effusion
- Asthma
- Pulmonary trauma, hematomas
- Inhalation injury
- Mucus plugs
- Bronchogenic carcinoma (other tumors)
PIOPED STUDY

- 933 recruited
- PE → 251 (33%)
- High probability    88% had PTE
- Intermediate probability    33% had PTE
- Low probability    12% had PTE
- Normal Scan excluded PE

[JAMA 1990; 263: 2753-59]
Systematic review and meta analysis of strategies for Dx of suspected PTE

Roy PM et al

- 48 articles analyzed
- 11004 pts with suspected PTE
- 3329 pts had PTE (30% prevalence)
- Mod. – High pre-test probability

High Probability V/Q
- Spiral CT +ve
- CSG +ve

\[ > 85\% \text{ post test probability} \]

- Low clinical probability – above results req. confirmation by Pul. Angio.
Low – Mod clinical Probability
- Negative quantitative D-Dimer test (<500μg/L)
- Spiral CT –ve
- CSG –ve
- Normal/near normal lung scan

High clinical probability → above results req. confirmation by Pul. Angio.

BMJ 2005; 331: 259-63
V/Q scan & Helical CT in Suspected PTE

Hayashino et al

- Meta analysis of Dx performance
- 12 article included
- Pooled sensitivity for Helical CTPA – 86%
  Specificity – 94%
- V/Q scan – High probability Normal
  Sensitivity 39% 98.3%
  Specificity 97% 4.8%

Conclusion:
- Helical CT has greater discriminatory power than V/Q scan with (N) threshold to exclude PTE
- Helical CT & V/Q scan with high probability – Similar discriminatory power in Dx. of PTE
Use of Ga$^{67}$ declined over last decade

Reasons:
- Lack of specificity
- Delay between injection and imaging time
- Relatively poor imaging characteristics

PET/SPECT has replaced Ga scans as tumor imaging agent of choice
MECHANISM OF UPTAKE:
TUMOR & INF./INFL.

Gallium – 67 Citrate

- Used since 1869
- Acts as Iron analogue
- Transported in blood bound to transferrin
- Tumors:
  - ↑ transferrin receptors in malignant cells,
  - ↑ Ga – transferrin binds to these receptors
  - Ga incorporated in intracellular lysosomes
  - ↑ Lactoferrin levels in lymphoma (Lactoferrin binds to Ga)
Inflammation

- ↑ lactoferrin levels in leucocytes & abscess fluids
  ∴ ↑ Ga uptake in infl. conditions

[Lactoferrin released by leucocytes & Bacteria]
- Highly conc. in sub-acute/chr. inf./infl. than acute processes

Normal Distr.

- Liver/spleen/skeletal system/colon
  varying degrees: salivary / lacrimal glands, nasal region, genitalia
- Excreted: bowels – 80%
  kidneys – 20%
Study Performed

- $\text{Ga}^{67}$ IV 8-10mCi
- Whole body/localized imaging after 24-48hrs
- Imaging can be repeated up to 96-120hrs.

Pt. Preparation

- No dietary restr.
- No BT/Gad MRI in previous 24hrs. : interfere with normal $\text{Ga}^{67}$ distr.
Thalium-201 Chloride

Mech. Of uptake
- Analogue of K\(^+\) uses ATP pump
- Co-transport mech. in tumor cells inv. K\(^+\), Na\(^+\), Cl\(^-\)
- Leaky capillaries

Mainly accumulates at sites of tumor
Min. uptake in infl. focus

Study performed
- TI201 IV 3-5mci
- Imaging started at 20min. and continued to 60min.
- Lymphoma, kaposi’s sarcoma
  ↓
  - Delayed images
**Pt. Preparation**

- 4 hrs. fasting (to min. salivary and splanchnic uptake)
- Avoid physical exertion for at least 4 hrs. (to min. skeletal muscle and cardiac uptake)
- (N) uptake – liver/heart

**Clinical Application**

- Diff. between benign/malignant disease
- Grade of malignancy
- Response to therapy/Recurrence
Technetium 99m Sestamibi

- Useful identifying primary tumor: Parathyroid adenoma, Breast, lung, bone, brain
- Uptake depends on blood flow/leaky capillaries/↑Permeability

Neuroendocrine Imaging Radiotracers

- Used for imaging Pheochromocytomas, carcinoid tumors, neuroblastoma and other neuroendocrine tumors
- Carcinoid tumors: $^{123}$I MIBG – 80% sensitive
- $^{123}$I-MIBG : 10mCi IV followed by whole body imaging at 24 hrs.
**Pt. Preparation**
- KI (2dr. BD) x 1-3 days
- No dietary restr.

**Octreoscan**
- Tumors esp. endocrine – high density of somatostatin receptors
- In$^{111}$ labelled somatostatin analogue effectively localizes tumor
- Tc$^{99m}$ depreotide (Neotect), somatostatin receptor binding agent helpful in evaluation of Pul. Nodules
- 6mCi IV – Whole body imaging – 6hrs. & 24hrs.
- Well hydrated
**Gallium in Cancer**

- Most avid uptake in lymphoma/Lung cancer/sarcoma/melanoma

**Lymphoma**

- Staging

<table>
<thead>
<tr>
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<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>HD</td>
<td>86-97%</td>
<td>100%</td>
</tr>
<tr>
<td>NHL</td>
<td>86-92%</td>
<td>100%</td>
</tr>
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- Residual disease

<table>
<thead>
<tr>
<th></th>
<th>Ga Scan Vs CT thorax</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>96% 68%</td>
</tr>
<tr>
<td>Specificity</td>
<td>80% 60%</td>
</tr>
</tbody>
</table>
– Specificity reduced by inflammatory changes (benign activity lower than malignant activity more often B/L and symmetric)

**TI$^{201}$ Vs Ga$^{67}$**

– Good tool to evaluate malignant bone lesions
  - Sensitivity – 88%
  - Specificity – 94%

– Inferior to Ga in staging lymphoma
Lung Cancer
- Ga has high affinity for lung cancer
  Sensitivity: 85 – 97%
- Superseeded by FDG for tumor identification staging
- Absence of FDG availability: Response to therapy
- Neotect useful in SPN evaluation
  Sensitivity: 97%
  Specificity: 73%

Mesothelioma
- Ga reliable for assessing extent of Pleural invasion
  Only when Pleural thickening > 6mm
**Carcinoids**

- Don’t take up Ga, FDG
- Octreoscan and I$^{123}$ MIBG used
- Useful for staging

**In summary**

- With advent of PET
  - Role of Ga in staging response to therapy – Has reduced
- Useful when there is no access to PET
Inflammation/Infection

- Ga uptake generally associated with cellular infiltration rather than fibrosis

- Sarcoidosis: signs on Ga scan that suggest Dx
  - Lambda Sign: Rt. Paratracheal, B/L Hilar adenopathy resembles letter lambda
  - Panda Sign: Uptake in B/L lacrimal & parotid glands resembles panda bear

- Either or both of these patterns on Ga scan with symmetric B/L Hilar LNE or B/L interstitial opacities are highly sensitive & specific for sarcoidosis however,

- Ga scan in isolation 48% overall diagnostic sensitivity
Panda Pattern may be seen
- HIV
- Sjogren’s syndr.
- RA
- SLE
- Head & neck RT for lymphoma

Uptake due to
- ↑ Capillary permeability
- In corporation by activated infl. cell

Various studies: Sensitivity of Ga scan for Dx 60-90% with poor specificity

Ga scan helpful in cases when Bx is necessary for Dx but Pt. is a poor candidate for FOB→ extra thoracic site identification for safer Dx Bx
Combination of negative Ga scan & SACE levels virtually excludes the Dx of sarcoidosis

Ga scan more sensitive than SACE in identifying pts. with active sarcoidosis

Clinical scenarios in which Ga scan is useful:

- Assisting in Dx of difficult cases esp. those with isolated extra-thoracic disease
- Identify active sites for Bx
- Differentiating active disease from fibrosis in a lung transplant candidate
Drug toxicity & Radiation pneumonitis
- Routine use not recommended
- May precede CXR changes
- Useful in establishing Dx in difficult cases
- Not very sensitive in Ac. Radiation Pneumonitis

Infl./Occupational/Chr. Lung disease
- Ga uptake sec. to - Ac. Infl. Component
  - ↑Alveolar capillary permeability
- Asbestosis: Ga uptake +ve in pts. With (N) CXR
  - HRCT +GA scan: Helpful when clinical exam, CXR, PFT equivocal
CVD: Ga scan may provide estimation of location of inflammation & help guide BAL/Bx

Not routinely used

Summary

- Ga scan sensitive indicator of non-infectious, infl. lung disease
- However, not specific, inconvenient imaging necessitating multiple visits to Nuclear Med. Dept.

Relegated to problem solving role rather than routine practice
Infectious Disease

- **TB**
  - High sensitivity for detection of active disease
  - Helpful in differentiating active disease from fibrosis

- **Other pul. inf:** Difficult situations where infection not readily apparent (PUO)

- **Ga scan preferred over WBC scan in leucopenic pts., pediatric population**

**AIDS**

- Diffuse Ga uptake in PCP has high sensitivity (80-96%) but poor specificity

- Negative Ga scan in pts. with (N) CXR has high negative predictive value in excluding Pul. disease

- Not routinely in PCP w/u
Reasons: Poor specificity
Delayed imaging (24-48hrs)
HRCT favoured (sensitivity-100%, specificity-89%, accuracy-90%)

Ga scan reserved for situations where sputum analysis/BAL/HRCT – Non-diagnostic, empiric therapy not preferred

A negative Ga scan with abnormal CXR highly suggestive of Kaposi sarcoma as KS is not Ga avid

CMV mimics PCP but may have accompanying adrenal, lacrimal, colonic inv.
Pul. & Parotid uptake (+) LIP
Pul. & skeletal uptake (+) actinomycosis/nocardia
Summary

- Not used routinely
- Used occ. in distinguishing active diseases from scarring or when there is no other source of infection apparent
LUNG CANCER

Single Photon Radionuclide Imaging in Lung Cancer

- Despite the emergence of PET – widely accepted
- Interest remains in single photon techniques
  - Because COZ
- Wide availability of single photon equipment
- Ga$^{67}$ – Not useful in detecting lesions < 1.5cm
  - False negative scan in upto 22% pts. of lung ca.
  - High PPV, low NPV
- Specificity for med. staging – 38-100%
  - No current role for characterization of SPN & staging of lung ca
**TI$^{201}$**
- Like Ga cannot detect lesions <2cm
- Poor imaging characteristics
- Not widely accepted in assessment of SPN

**Tc$^{99m}$ tetro fosmin, Tc$^{99m}$ – MIBI scan**
- < 1cm lesions – Poor sensitivity
- Poor to FDG-PET in primary tumor visualization & detecting med. lymph mode metastasis

**Somatostatin receptor imaging**
- High affinity somatostatin receptors (+) variety of malignancies including SCLC
- Lower frequency of expression in NSCLC
- NSCLC constitutes majority of lung cancer
  ∴ This may hamper detection of malignancy within SPN
- However studies showed sensitivity of upto 96% in lung cancer detection
PET in NSCLC

Basics

- FDG is a glucose analogue
- Facilitated transport into cells via glucose membra. transporter [GLUT-1 to GLUT-7]
- Within the cells
  FDG
  ↓ Phosphorylation by hexokinase
  2 deoxy-glucose-6- Phosphate (Accumulates as no further metabolism takes place)
NSCLC

- Increase in GLUT-1, and GLUT-3 expression
- ↑ glucose use by tumor cells
- Upregulation of hexokinase levels, down regulation of glu-6 phosphatase
- Deoxyglucose retention within cells
SPN

- 20-50% malignant
- **Existing diagnostic modalities**
  - Radiology: Benign etiology suggested by
    - Prolonged stability
    - Smooth control
    - Calcification: Central/diffuse/Laminated/Popcorn
  - However, majority of SPN after CT, remain indeterminate
  - Dual energy CT/contrast enhanced dynamic CT
    - Sensitivity: 98%
    - Specificity: 58%
- **Histologic sampling**
  - Indeterminate lesions
    - Obtain tissue Bx
- **FOB: cytology & Bx**
  - ↑ yield for
    - central lesions
    - endobronchial component
    - Bronchus entering prox. part of lesion
- **TTNB:**
  - Better for – Peripheral lesion,
    - FOB not available
  - Sensitivity – 71-100%
  - complications – Pneumothorax (61%)
    - 5-27% req. ICT
    - Haemorrhage
Thoracoscopy
- Peripheral lung lesions
- Complications: Mean hospital stay 2.4-5.7 days
  : Duration of ICT: 1.8-3.3 days

Open thoracotomy
- No definitive Dx. inspite of all less invasive diagnostic procedures
FDG PET
- Sensitivity : 83-100%, Specificity : 52-100%
- PPV : 92.6%, NPV : 87%
- Accuracy : 91.3%

FDG-PET is more sensitive & Specific in characterization of SPN than any other currently available non-invasive method

Either semi-quantitative/visual methods used for diff. bet benign & malignant SPN

Most common semi-quantitative measurement is standard uptake value [suv]

SUV of 2.5 at 1hr used to diff. bet benign and malignant SPN
False positive cause of FDG are pred. inflammatory in origin

Causes of False-Positive Findings with FDG-PET for characterization

Granulomas
Histoplasmosis
Tuberculosis
Schwannoma
Chronic inflammation
Aspergillus infection
Abscess
Acute blastomycosis
Sarcoidosis
Cryptococcus neoformans
Wegener’s granulomatosis
Aggressive neurofibroma
Coccidiodomycosis

False negative: small size (0.5cm)
well diff. malignancies (carcinoids, well diff. adeno ca, BAC)
Current clinical algorithm for the use of FDG-PET in characterization of SPNs

- SPN confirmed on CT
  - Low probability of malignancy → Watch and Wait
  - Intermediate Probability of malignancy → Attempt biopsy
  - High probability of malignancy → Investigate & treat as lung cancer

- Benign pathology
- Indeterminate of non diagnostic biopsy → FDG PET
- Malignant
- Negative – Serial radiology
- Positive malignant
Accuracy of PET for Dx of Pul Nodules/Mass

Gould MK et al

- Meta analysis
- 40 studies
- 1474 focal pul. lesion
- Sensitivity/specificity – 91.2%
- In current practice: Sensitivity-96.8% Specificity-78%
- No diff. in Dx. accuracy of Pul nodules C/w lesion of any size

Conclusion:
- Accurate non-invasive imaging test for Dx of Pul. Nodules/Mass lesion

JAMA 2001; 285: 914-924
Summary of Major Studies on FDG-PET in Characterization of SPN

- Studies between 1990-2001
- 2079 pts
- 73.1% malignant lesions
- Sensitivity - 95.9%
- Specificity – 79%
- PPV – 92.6%
- NPV – 87%
- Accuracy – 92%

Seminars in Nucl. Med. 2002; 240-271
STAGING OF NSCLC

Existing Staging Procedures

CT

- Useful in T staging
- N stage esp. mediastinum inv. Node >1cm in short axis
- By using above criteria
- CT has sensitivity – 78%
- Specificity – 79% for LN mets
- CT may over/under stage upto 40% pts.
- Useful in detection of distant mets
- Cerebral CT: if clinical exam reveals focal neurodeficit on finding of disseminated disease
If solitary lesion identified – Bx preferred in v/o false positive (11%)

Bone Scan: Skelatal mets identification

Mediastionoscopy
- Inoperable cases
- Large Med. LNE
  Complications – 23%
  False Neg. – upto 10%
- TBNA
  Sensitivity – 53%
  Specificity – 99%
  Complications – Haemorrhage
    – Pneumomesmediastinum
Other Modalities
- MRI useful for staging med LNE
- Useful in assessment of indeterminate adrenal masses

FDG-PET Staging the Primary
- Poorly suited to assess the stage of primary tumor (T).
- CT better suited → Reason: Better resolution, provides more anatomic detail

Staging the mediastinum
- Sensitivity : 83.3%
- Specificity : 92.2%
- False positive usually d/t inflammatory pathology
Causes of False-Positive findings in FDG-PET thoracic Lymph node staging

- Bronchiectasis
- Upper respiratory tract infection/bronchitis
- Rheumatoid disease
- Proximity of tumor to mediastinum
- Pneumoconiosis
- Anthracosis/silicoanthracosis
- Hyperplastic lymph node/reactive hyperplasia/active
- Inflammation/Nonspecific inflammation
- Aspergilloma with reactive nodes
- Active granulomatous disease
- Active inflammation due to poststenotic pneumonia
False Positive $\rightarrow$ Relatively infrequent, may result in denying a pt. potentially curative Sx

$\downarrow$

$\therefore$ Recommended: Invasive Sx staging

False Negative

- Nodes immediately adjacent to primary tumor
- 2 or more LN adjacent to each other but at diff. LN stations $\rightarrow$ PDG-PET not able to resolve them separately
- Normal size nodes with microscopic foci of tumor
Assessment of Distant Metastasis

- Able to detect 94% distant mets
- Superior in detection of distant mets c/w other modalities
- FDG-PET relatively insensitive for cerebral mets
  Reason: High Background caused by normal cerebral FDG uptake
  [CT/MRI considered superior]
- Osseous mets: Bone scintigraphy vs FDG-PET
  - Sensitivity 90% 90%
  - Specificity 66% 98%

Adrenal mets: for indeterminate lesions
- Sensitivity 80% and Specificity 80%
Hepatic mets
- Able to detect unsuspected hepatic mets
- Characterizes the hepatic abnormalities identified on CT

Management Change
- Several studies have reported an overall management change between 24-40%

Cost effectiveness
- Major potential for cost saving is via
  - Minimizing invasive staging of mediastinum
  - Avoidance of inappropriate Sx in those with inoperable locally invasive or metastatic disease

FDG-PET is most cost effective when performed on pts. With CT negative for nodal metastases with Bx to confirm PET positive results
Current clinical algorithm for use of FDG-PET in staging of NSCLC

- Proven or presumed NSCLC operable or equivocally operable on CT

  - PET Negative
    - Surgery
  - PET positive in mediastinum
    - Mediastinoscopy
      - Malignant Nodes
        - No surgery-chemotherapy radiotherapy
      - Biopsy negative for metastatic malignancy
        - Biopsy positive for metastatic malignancy
          - Biopsy positive for metastatic malignancy
            - Palliation
          - Biopsy negative for metastatic malignancy
            - Surgery (if mediastinum negative)
      - No malignant Nodes
        - PET positive for distant metastases
          - Biopsy
            - Biopsy negative for metastatic malignancy
              - Surgery (if mediastinum negative)
            - Biopsy positive for metastatic malignancy
              - Biopsy positive for metastatic malignancy
                - Palliation
          - Biopsy negative for metastatic malignancy
            - Surgery (if mediastinum negative)
        - No surgery-chemotherapy radiotherapy
      - Malignant Nodes
        - No surgery-chemotherapy radiotherapy
    - Biopsy negative for metastatic malignancy
      - Surgery (if mediastinum negative)
    - Biopsy positive for metastatic malignancy
      - Biopsy positive for metastatic malignancy
        - Palliation
    - Biopsy negative for metastatic malignancy
      - Surgery (if mediastinum negative)
  - PET positive for distant metastases
    - Biopsy
      - Biopsy negative for metastatic malignancy
        - Surgery (if mediastinum negative)
      - Biopsy positive for metastatic malignancy
        - Biopsy positive for metastatic malignancy
          - Palliation
    - Biopsy negative for metastatic malignancy
      - Surgery (if mediastinum negative)
  - PET negative
    - Surgery
Test performance of PET and CT for mediastinal staging in pts. With NSCLC

- Meta analysis
- 39 studies
- 1959 pts

Mediastinal staging
- CT
- FDG-PET
  - Sensitivity: 61% vs. 85%
  - Specificity: 79% vs. 90%

PET more sensitive & less specific where CT showed enlarged nodes [100% & 78%] than when CT showed no LNE [82% & 93%]

Conclusion
- FDG PET more accurate than CT for Med. Staging
Utility of Tc\textsuperscript{99m} Depreotide C/W FDG-PET & surgical staging in NSCLC

Kahn D et al

- 166 pts
- Detection of malignant disease
  - Sensitivity
    - PET: 96%
    - Tc\textsuperscript{99m} depreotide: 94%
  - Specificity
    - PET: 71%
    - Tc\textsuperscript{99m} depreotide: 51%
- FDG-PET correctly stage 55% of pts C/W Tc\textsuperscript{99m} depreotide (45%)

Conclusion
- Sensitivity equal for both modalities
- Specificity superior for PET

Chest 2004; 125: 494-501
Utility of PET in staging potentially operable NSCLC

Reed C et al

303 pts, 22 institutions underwent PET after routine staging

Detection of PET CT

N₁ 42% 13%
N₂/N₃ 58% 32%

NPV for Med. node – 87%
Mets identified in 6.3%

Conclusion:
– PET prevents non-therapeutic thoracotomies
– +ve finding confirmed by mediastinoscopy
– Mets require confirmation by biopsy

J Thorac Cardiovasc Surg 2003; 126: 1943-51
Delayed FDG-PET scan for Diff. between malignant and Benign lesions

Nakamoto Y et al

- 47 pts suspected pancreatic Ca – PET scan
  - Malignant: 27
  - Benign: 20
  - SUV at 2hrs. ↑22 lesions, ↓17 lesions
  - SUV cut off of 2.5 – 1 false –ve, 7 false +ve
  - Dx accuracy – 83%

- Delayed FDG-PET scan at 2hrs post inj. May help diff. between benign and malignant lesions

Cancer 2000; 89: 2547-54
Detection of Recurrent disease

- Sensitivity: 97-100%
- Specificity: 61.5-100%

False positive results

- Radiation pneumonitis [preferable – wait for 6mths
  Atleast – 3mths after completion
  of RT before performing PET scan]

False positive uptake declines with time

↓

∴ Some role of repeating PET scan if false +ve suspected
[curvilinear uptake S/o false +ve]
PET IN NON-MALIGNANT THORACIC DISORDERS

Pnemoconiosis

- FDG-PET studies revealed ↑ uptake
- ↑ uptake d/t infl. Cell – macrophages, fibroblasts
- Specific radiotracer that localizes to fibroblasts and not in infl. Cell: 18F-fluoroproline
- Fluoroproline – PET studies → ↑ uptake in early fibrosis
Infection/Inflammation

- Infl. Cells at site of infl./inf. show ↑ FDG uptake
- Infl. Cells show lower level of FDG uptake C/W malignant cells
- ↑ uptake is d/t
  - ↑ GLUT expression
  - Cytokines & growth factor ↑ affinity of GLUT to FDG
- Sensitivity: 92%, Specificity: 100% in infl./inf. lesions

AIDS

- Major role of PET imaging
- Identify correct location for further inv. Bx, Aspiration, or other modalities
- Sensitivity & specificity of PET in localizing lesions in AIDS pts. 92% & 94% respectively
FUO

- Useful tool in this setting
- Identifies lesions responsible for fever in >50% of pts.
- FDG-PET compares favourably with Ga$^{67}$ studies in PUO evaluation
- FDG-PET may replace Ga$^{67}$ as it gives quicker results
Sarcoidosis

- Useful in Mx of Pts with sarcoidosis
- CXR Ab. (N) ↑ACE levels with (N) PET → may remain well without t/t
- Not useful in Dx as findings may be confused with lymphoma

Monitoring disease process and response to therapy

- FDG-PET useful for this purpose in TB/Aspergillosis Alveolar echinococciosis /MAI
Role in pleural disease

- Useful in Dx & Staging of malignant mesothelioma
- Useful to determine whether there is malignant transformation of reactive pleural disease
- More accurate than CT to identify extent of disease, stage of disease in mediastinum, detect occult extra thoracic metastasis
- FDG-PET can be use to diff. benign from malignant Pl. thickening and for Dx & staging of mesothelioma
- Study can identify other focal area of metastasis or even primary in pts. with malignant Pl. effusion with unknown primary tumor
- Alternate diagnostic method to invasive tests in suspected malignant Pl. effusion esp. in pts. with equivocal findings on CT/Negative finding on pl. cytology after thoracocentesis