PET CT for Staging Lung Cancer

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Disclosures

Neither I nor my immediate family members have financial relationships with commercial organizations that may have a direct or indirect interest in the content.
Intended Learning Objectives

- Introduction to hybrid imaging
- PET-CT in Lung Cancer
  - Assessment-Solitary Pulmonary Nodule
  - Staging of lung cancer- 8th Edition of TNM
  - Pitfalls & Limitations of PET-CT Imaging
- PET-CT with intravenous contrast
- Take home message-learning points
Introduction to Hybrid Imaging

- $^{18}\text{F}]$FDG PET-CT
- Cervical lymph node metastasis

**Anatomical**
- Location
- Size
- Density

**Functional**
- Time-course of metabolism

**Fusion**

**Hybrid imaging**

- Enhances
  - Image interpretation
  - Diagnostic accuracy

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Scanning Technique

CT images are obtained in ‘shallow/quiet breathing’

Currently most PET-CT protocols without IV contrast
PET-CT Images

MIP

FUSED

NAC
The mediastinal blood pool will typically have an SUV max in the range 1.5 - 2.5

There is no consensus, but in general one of two methods are used:

<table>
<thead>
<tr>
<th>Descriptor of activity</th>
<th>Absolute values</th>
<th>Blood pool values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low intensity</td>
<td>0-2.5</td>
<td>&lt; or = to mediastinal blood pool</td>
</tr>
<tr>
<td>Moderate intensity</td>
<td>2.6-5.0</td>
<td>&gt; mediastinal blood pool but &lt; or = background liver</td>
</tr>
<tr>
<td>High intensity</td>
<td>5.1-10.0</td>
<td>&gt; liver (up to 2x)</td>
</tr>
<tr>
<td>Very high intensity</td>
<td>&gt;10.0</td>
<td>&gt; liver (&gt;2x)</td>
</tr>
</tbody>
</table>

SUV max values allow semi-quantitative assessment for comparison with future studies, however subjective evaluation is also as valid.
Indications for FDG PET-CT in Lung Cancer

- **Characterisation** of a solid solitary pulmonary nodule
- **Staging** of patients considered for radical treatment of non-small cell lung cancer
- Assessment of **response** to chemotherapy and-or radiation treatment
- Assessment of suspected disease recurrence
- Staging of patients with **small-cell lung cancer** with limited disease on CT being considered for radical therapy

Solitary Pulmonary Nodule (SPN)

- A single spherical lesion of 3cm or less in diameter completely surrounded by lung parenchyma without any associated atelectasis or lymphadenopathy

**Pulmonary nodule**

- **Solid**
- **Sub-solid nodule (SSN)**
- **Part-solid nodule (PSN)**
- **Pure ground-glass nodule (PGGN)**

- Risk of malignancy is higher in PSN than PGGN or Solids
- PET/CT is not used to assess PGGN due to unreliability

**References**

- DP Naidich et al. Recommendations for the Management of Subsolid Pulmonary Nodules Detected at CT
# PET/CT assessment - SPN

<table>
<thead>
<tr>
<th>SPN</th>
<th>Size</th>
<th>Calcification</th>
<th>Growth</th>
<th>Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>&lt;0.7cm (1%)</td>
<td>Diffuse Central Laminated Popcorn</td>
<td>Stability over 2 years</td>
<td>Smooth</td>
</tr>
<tr>
<td>Intermediate</td>
<td>0.8-2cm (15%)</td>
<td>Other</td>
<td>Slow growth over 2 years</td>
<td>Lobulated</td>
</tr>
<tr>
<td>Malignant</td>
<td>&gt;2cm (75%)</td>
<td>Usually none</td>
<td>Rapid growth</td>
<td>Spiculated</td>
</tr>
</tbody>
</table>

**References**

- [Indeterminate Solitary Pulmonary Nodules Revealed at Population-Based CT Screening of the Lung: Using First Follow-Up Diagnostic CT to Differentiate Benign and Malignant Lesions. Takashima et al. AJR 2003; 180:1255-1263](https://pubmed.ncbi.nlm.nih.gov/12772101/)
- [Small Solitary Pulmonary Nodules (1 cm) Detected at Population-Based CT Screening for Lung Cancer: Reliable High-Resolution CT Features of Benign Lesions. Takashima et al. AJR 2003; 180:955-964](https://pubmed.ncbi.nlm.nih.gov/12772104/)
## Solitary pulmonary nodule (SPN)

### Performance characteristics of diagnostic tests for SPN

<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT scan</td>
<td>96% (91-98%)</td>
<td>50% (41-58%)</td>
<td>74%</td>
<td>Localisation Detection</td>
</tr>
<tr>
<td>FDG-PET</td>
<td>96.8%</td>
<td>77.8%</td>
<td>74%</td>
<td>Cost effective False +ve/-ve</td>
</tr>
<tr>
<td>PET-CT</td>
<td>97%</td>
<td>85%</td>
<td>93%</td>
<td>Synergistic</td>
</tr>
<tr>
<td>FNA-biopsy</td>
<td>80-95%</td>
<td>50-88%</td>
<td></td>
<td>Not always safe &amp; practical</td>
</tr>
</tbody>
</table>

Initial approach to solid and part-solid pulmonary nodules

Solid non-calcified nodule(s) on CT
- Clear features of benign disease, or nodule <5mm diameter (or <80mm) or patient unfit for any treatment?
  - Yes: Discharge
  - No:
    - Previous imaging?
      - Yes: Assess risk of lung cancer according to surveillance algorithm 2
      - No:
        - Nodule <8mm diameter or <300mm$^3$ volume?
          - Yes: Discharge
          - No:
            - Assess risk using Brock model
              - <10% risk of malignancy: CT surveillance (algorithm 2)
              - ≥10% risk of malignancy: PET/CT with risk assessment using Herder model (provided size is greater than local PET/CT threshold)

Part-solid nodule
- Solid component <10mm
- Solid component >10mm
  - Either serial thin slice CT surveillance or straight to resection dependant on patient factors
  - Consider excision or non-surgical treatment (+/- image-guided biopsy)
# Solitary pulmonary nodule (SPN)

## Whom to Image?
- Biopsy not safe or practical
- Pre-test probability-predictive models

### Patient Characteristics
- h/o smoking or malignancy
- Patients age

### Nodule Characteristics
- Nodule size and Location
- Morphology of nodule
  - Part solid and spiculated edges

## How to Interpret?
- Visual Assessment of Uptake
  - Absent, Faint, Moderate, Intense
- SUVmax values
- NAC vs AC images
- Previous and current CT (external)

YE Huang et al Nucl Med Commun. 2010 Nov;31(11):945-51
SPN: Lung Cancer

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PET CT ASSESSMENT- SOLID SPN

Round Atelectasis
Solitary pulmonary nodule (SPN)

As a general rule most malignant lesions have a higher level of glucose metabolism but this is not absolute

**False negatives**

- Low grade adenocarcinomas
- Carcinoids
- Tumours <1cm

**False positives**

- Tuberculosis
- Sarcoidosis
- Histoplasmosis & Wegner’s

Despite the above the FDG PET-CT for SPN characterisation is currently seen as arguably the most cost effective modality

Low SUV max & increased surgical risk-monitoring over time

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Pulmonary Carcinoid

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Adenocarcinoma spectrum

Preinvasive lesions (GGN)
- Adenocarcinoma in situ (AIS)
- Atypical adenomatous hyperplasia (AAH)

Minimally invasive
- Minimally invasive adenocarcinoma (MIA)

Invasive adenocarcinoma (Lung Mass)

References

- Gardiner et al. J Thorac Dis 2014;6 (s5) 537-546 (link??)
PET/CT assessment – Part-solid SPN

- Part-solid SPNs are part of the adenocarcinoma spectrum
- The development of solid components within a ground-glass nodule warrants further investigation
- The risk of malignancy increases with enlargement and increasing solidity
- Proposals for the 8th edition TNM classification advise measuring the largest diameter of the solid FDG-avid component of the nodule for T assessment
- This correlates with the pathological invasive component
Staging of Lung Cancer

- Jan 2018 8th edition of TNM classification
- Improve staging system, more accurate prediction of prognosis and better guide the treatment options.

Summary of changes
- AIS, T1mi

- T1: subdivision into T1a, T1b, T1c at 1cm intervals from <=1cm to <=3cm

- T2: subdivision into T2a and T2b at 1cm intervals from >3cm to <=5cm, endodronchial lesions <2cm from carina (downstaged), tumours with complete atelectasis
Staging of Lung Cancer

Summary of changes

- **T3:** >5cm but <=7cm
- **T3:** Invasion of mediastinal pleura is no longer a predictor
- **T4:** >7cm, invasion of diaphragm (upstaged)
- **M1b:** single extrathoracic metastasis in a single organ
- **M1c:** new category, multiple extrathoracic metastases in one or multiple organs
Role of PET-CT: T Stage

• **Accuracy: PET-CT (82%); PET (55%); CT (68%)**
  

• More accurate size measurement if adjacent atelectasis
  
  D Pawaroo et al AJR Am J Roentgenol. 2011;196:1176–81

• Increased accuracy of chest wall / mediastinal infiltration
  

• Pleural Invasion and malignant pleural effusion
  

• Improved lesion characterisation
  • Scarring vs tumour vs round atelectasis
  • Satellite nodules vs post obstructive changes

• Synchronous tumours / unexpected malignancies
Role of PET/CT: T stage

CT

PET
Role of PET/CT: T stage

CT

- T2a
- T1b

PET

<3cm

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Role of PET/CT: T stage

CT

- T2a
- T1b

>3cm

PET

<3cm

Fused
Role of PET/CT: T2 disease

Peripheral pleural based lesions can be problematic and it can be difficult to distinguish between visceral pleural and parietal pleural or chest wall involvement.

- Pleurally based lesion
- Difficult to exclude parietal pleural involvement
- Pneumothorax which had elevated the visceral pleura
- Parietal pleura and chest wall were clear
- T2a disease
Chest wall Invasion
Role of PET/CT: T3 disease

Pericardial involvement

- Large partially-necrotic mass
- Extending to the pericardium
- Broad base of contact

- No extension of tumour into heart
- In keeping with T3 disease
T4 extension into left atrium
Recurrent laryngeal nerve – left vocal cord palsy

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Synchronous lung primary
Synchronous lung and laryngeal
Role of PET-CT: N Stage

• The identification of nodal involvement is vital to select candidates for curative surgery

• Conventional Imaging - poor accuracy
  • sensitivity: 60-83%; specificity: 77-82%
    BA Dwamena et al Radiology. 1999;213:530–6
  • 44% metastatic nodes were <1cm
  • 77% without metastatic nodes had a node > 1cm

• PET-CT higher diagnostic accuracy
  • very high negative predictive value (91%) and specificity (83%)
  • sensitivity 32.4% in nodes <10 mm & 85.3% in nodes ≥10 mm
Relevant Anatomy

“Elementary, my Dear Watson!”
Use the buttons to explore scan images detailing the locations of the nodal zones and stations. Click the zone names to view related slices; the eye buttons will reveal the relevant stations on the diagram.
Current best practice in staging

Lung Cancer: The diagnosis & treatment of lung cancer

Issued: April 2011

NICE clinical guideline 121

CT thorax, upper abdomen & lower neck with intravenous contrast administration

No

Nodal status influences management or is source of diagnosis?

Yes

Mediastinal sampling not indicated

Peripheral lesion without enlarged mediastinal nodes (10mm short axis: low probability of malignancy)

PET/CT if suitable for potentially curative treatment, otherwise skip this step

Transthoracic needle biopsy

Peripheral or central lesion with enlarged lymph nodes that may determine treatment with curative intent

Mediastinal nodes 10-20mm short axis (i.e. intermediate probability of malignancy)

Mediastinal nodes >20mm short axis (i.e. high probability of malignancy)

EBUS/EUS

Bronchoscopy & non-US-guided TBNA if nodes are present or lesion is submucosal

Surgical biopsy/definitive resection ± mediastinal sampling (may included combined EBUS & EUS) and PET/CT if not already done. Consider this option at any stage in the pathway

Diagnosis & stage

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Key points of NICE guideline

• PET-CT preferred 1st test after CT if low probability mediastinal involvement (nodes <10mm short axis)
• PET-CT or EBUS TBNA or EUS FNA if intermediate probability (nodes between 10-20mm short axis)
• Neck US if high probability (nodes >20mm short axis)

Low probability  
Nodes <10mm short axis

Intermediate probability  
Nodes 10 to 20mm short axis

High probability  
Nodes > 20mm short axis
Role of PET-CT: N Stage

• Histological confirmation should be performed in all considered for surgery or radical RT if PET-CT is +ve

• Histological/cytological confirmation is not required
  • Definite distant metastatic disease
  • PET-CT for N2/N3 disease is -ve even if nodes enlarged on CT
  • High probability that the N2/N3 disease is metastatic

• Valuable information about inaccessible nodal stations
  • Modifying mediastinoscopic approach / other methods
  • PET-CT virtual mediastinoscopy-useful adjunct

Chain of avid mediastinal nodes
Role of PET-CT: N Stage

SUVmax ratio ≥ 0.2 (0.63). This was biopsy positive

SUVmax ratio < 0.2 (0.18). This was biopsy negative
Role of PET-CT: M Stage

- 18-36% distant metastases at presentation
- Common sites: adrenal glands, bones, liver & brain
- 20% relapse due to undetected micrometastasis
- Detects clinically unsuspected distant metastases in up to 28%
- Reduction in futile thoracotomies

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>CWU</th>
<th>FDG-PET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I &amp; II</td>
<td>46%</td>
<td>25%</td>
</tr>
<tr>
<td>Stage III</td>
<td>29%</td>
<td>11%</td>
</tr>
</tbody>
</table>

*H van Tinteren The PLUS multicentre randomised trial. Lancet. 2002;359:1388–93*

- Cost effective staging modality and help in targeting biopsy

M staging: adrenals

Role of PET/CT in adrenal metastasis - Brady et al

- 187 adrenal nodules in 147 patients

- Combination of CT density value (10 HU cut-off) and an absolute SUV max value (3.1 cut-off for malignant lesions)
  - 97.3% sensitivity, 86.2% specificity

- Combination of unenhanced CT density (>10 HU cut-off) and SUV ratio (adrenal:hepatic uptake > 1.0 cut-off)
  - 97.3% sensitivity, 74.1% specificity

- When SUV ratio of > 2.5 was used, 100% specificity was achieved in characterising adrenal lesions as malignant

Recommended reading

Adrenal metastasis
M staging: adrenals – example

- Left adrenal gland is enlarged
- This is not 2.5 times higher than hepatic SUV max value - therefore indeterminate

Findings

NCCT density = 14 HU
Adrenal SUV max = 3.4
Final true washout = 70%
Diagnosis: Benign adrenal adenoma
M staging: bones, brain and liver

Bone metastases:
- Metastases – range 8% to 34%
- Particularly useful for occult bone metastasis that are not picked up on CT, and are falsely negative on bone scans

<table>
<thead>
<tr>
<th></th>
<th>PET-CT</th>
<th>MRI</th>
<th>Bone scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>92%</td>
<td>77%</td>
<td>86%</td>
</tr>
<tr>
<td>Specificity</td>
<td>98%</td>
<td>92%</td>
<td>88%</td>
</tr>
</tbody>
</table>

Brain metastases:
- Metastases to the CNS detected in 18% of patients with M1 disease at presentation
- FDG-PET is not very useful due to increased FDG activity in normal brain
- These patients require contrast-enhanced MRI

Hepatic metastases:
- Can be seen on PET/CT - often superior to CT
- MR liver with contrast is the imaging modality of choice for segmental localisation and accurate assessment of the number of metastases

Recommended reading
Unexpected bony metastasis
Pitfall and Limitations of PET-CT

False Positives
- Physiological
- Inflammation/Infection
  - Sarcoidosis, TB, Wegeners
- Infarction
  - Embolus
- Iatrogenic
  - Pleurodesis
  - Post Treatment

False Negatives
- Small size
  - micrometastasis
- Low metabolic tumours
  - Carcinoid
  - Well diff adenocarcinoma
- Technical factors
  - Misregistration
  - Glucose serum levels
Sarcoidosis
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FDG Embolus

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Talc pleurodesis
PET CT - Misregistration
PET-CT: Intravenous contrast

- **Multiphase CT protocol**
  - low-dose non-enhanced attenuation scan
  - diagnostic contrast-enhanced scan
  - followed by a whole-body PET

- **Benefits**
  - Additional Diagnostic Information in 52/100 Patients
  - Improved Localisation of FDG uptake
  - Precise Tumour Delineation and Local staging

  Pfannenberg et al BJR 2007 80:437-445

- **Not routinely used?**
  - Attenuation correction artefacts
  - Hospital Logistics
  - Specific protocols-PET/CT reporting
IV PET-CT

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Conclusions

- PET-CT has established itself as an important step in the management of patients with lung cancer
- Useful in characterisation & risk stratification of SPN
- Definite role in staging Lung cancer
  - Most accurate and cost effective modality
  - Avoid futile thoracotomies and guide biopsies
- Must remember limitations of PET-CT
  - PET-CT stage is not the pathological stage
  - High negative predictive value-micrometastases
  - Histological confirmation of all suspected N2/N3 disease
- Role in RT planning, response monitoring, prognostication
THANK YOU