PET-CT in Staging Lung Carcinoma

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Consultant Radiologist
Intended Learning Objectives

• Introduction to hybrid imaging

• PET-CT in Lung Cancer
  • Assessment-Solitary Pulmonary Nodule
  • Revised staging of lung cancer (including 8th Edition of TNM)
  • Pitfalls & Limitations of PET-CT Imaging

• Advances and other uses of PET-CT
  • Use of IV contrast-one stop shop
  • 4D PET-CT
  • Prognostication, RT planning and Response Assessment
  • Novel Tracers other than FDG

• 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

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Solitary Pulmonary Nodule (SPN)

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

- The probability of lung cancer increases with tumour size.

- The incidence of malignancy in SPN varies widely (5-70%).

- Reliable characterisation frequently not possible on conventional radiological features – Invasive procedures.

## 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></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>

References:
# Solitary pulmonary nodule (SPN)

## Whom to image?
- Biopsy not safe or practical
- Pre-test probability-predictive models
- h/o smoking or malignancy
- Patients age
- Nodule size (>7mm)
- Morphology of nodule
  - Part solid and spiculated edges

## How to Interpret?
- Increased uptake
- SUV vs Visual assessment
- SUVmax values
- NAC vs AC images
- Previous and current CT (external)

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

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## 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.

SPN: Lung Cancer
Use of NAC in small nodules
Hamartoma

Lung Cancer

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Adenocarcinoma
Staging of Lung Cancer

• Importance of accurate initial disease staging
  • Crucial to correctly identify potentially curable disease

• In 2009 **TNM 7 staging system** (IUAC & AJCC)

**Key points**

• More accurate reflection of relationship with patient survival
• Applies to NSCLC, small cell and pulmonary carcinoid
• Subdivisions based on T size (long axis)
• New Lymph node map but no change in N classification
• Local metastases (M1a) and Distant metastases (M1b)
• PET-CT allows more accurate staging
Staging of Lung Cancer

- In 2016 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, 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
- **M1b**: single extrathoracic metastasis in a single organ
- **M1c**: new category, multiple extrathoracic metastases in one or multiple organs
# Staging of Lung Cancer

## Overview of the revised 7th edition of the TNM classification of lung tumours

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>Prior</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=2cm</td>
<td>T1</td>
<td>T1a</td>
</tr>
<tr>
<td>&gt;2 but &lt;=3</td>
<td>T1</td>
<td>T1b</td>
</tr>
<tr>
<td>&gt;3 but &lt;=5</td>
<td>T2</td>
<td>T2a</td>
</tr>
<tr>
<td>&gt;5 but &lt;=7</td>
<td>T2</td>
<td>T2b</td>
</tr>
<tr>
<td>&gt;7cm</td>
<td>T2</td>
<td>T3</td>
</tr>
</tbody>
</table>

### Pleural Invasion

<table>
<thead>
<tr>
<th>Pleural Invasion</th>
<th>Prior</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visceral Pleura</td>
<td>T2</td>
<td>T2a/b</td>
</tr>
<tr>
<td>Parietal Pleura</td>
<td>T3</td>
<td>T3</td>
</tr>
<tr>
<td>Mediastinal Pleura</td>
<td>T3</td>
<td>T3</td>
</tr>
<tr>
<td>Par. pericardium</td>
<td>T3</td>
<td>T3</td>
</tr>
</tbody>
</table>

### Central airway

<table>
<thead>
<tr>
<th>Central airway</th>
<th>Prior</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2cm from carina</td>
<td>T2</td>
<td>T2a/b</td>
</tr>
<tr>
<td>&lt;2cm from carina</td>
<td>T3</td>
<td>T3</td>
</tr>
<tr>
<td>Involving carina</td>
<td>T4</td>
<td>T4</td>
</tr>
</tbody>
</table>

### Lung atelectasis

<table>
<thead>
<tr>
<th>Lung atelectasis</th>
<th>Prior</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; entire lung</td>
<td>T2</td>
<td>T2a/b</td>
</tr>
<tr>
<td>Collapse entire lung</td>
<td>T3</td>
<td>T3</td>
</tr>
</tbody>
</table>

### Satellite Nodules

<table>
<thead>
<tr>
<th>Satellite Nodules</th>
<th>Prior</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same lobe</td>
<td>T4</td>
<td>T3</td>
</tr>
<tr>
<td>Same lung diff lobe</td>
<td>M1</td>
<td>T4</td>
</tr>
<tr>
<td>Contralateral Lung</td>
<td>M1</td>
<td>M1a</td>
</tr>
</tbody>
</table>
# Staging of Lung Cancer

## Overview of the revised 7th edition of the TNM classification of lung tumours

<table>
<thead>
<tr>
<th>Soft tissue invasion</th>
<th>Prior</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest wall &amp; Superior sulcus tumors</td>
<td>T3</td>
<td>T3</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>T3</td>
<td>T3</td>
</tr>
<tr>
<td>Mediastinum</td>
<td>T4</td>
<td>T4</td>
</tr>
<tr>
<td>Heart or Great Vessels</td>
<td>T4</td>
<td>T4</td>
</tr>
<tr>
<td>Trachea/Esophagus</td>
<td>T4</td>
<td>T4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Osseous Invasion</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Rib</td>
<td>T3</td>
<td>T3</td>
</tr>
<tr>
<td>Vertebral Body</td>
<td>T4</td>
<td>T4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nerve Invasion</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Phrenic nerve</td>
<td>T3</td>
<td>T3</td>
</tr>
<tr>
<td>Recurrent laryngeal</td>
<td>T4</td>
<td>T4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lymph node</th>
<th>Prior</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>No lymphadenopathy</td>
<td>N0</td>
<td>N0</td>
</tr>
<tr>
<td>Ipsilateral peripheral / hilar / interlobar zone</td>
<td>N1</td>
<td>N1</td>
</tr>
<tr>
<td>Ipsilateral upper, AP, lower and/or subcarinal Zone</td>
<td>N2</td>
<td>N2</td>
</tr>
<tr>
<td>Supraclavicular zone or contralateral nodes</td>
<td>N3</td>
<td>N3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Contralateral Lung</td>
<td>M1</td>
<td>M1a</td>
</tr>
<tr>
<td>Pleural/Pericardial</td>
<td>M1</td>
<td>M1a</td>
</tr>
<tr>
<td>Distant Metastases</td>
<td>M1</td>
<td>M1b</td>
</tr>
</tbody>
</table>

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Proposed Lymph Node Map


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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
Identification of central obstructing tumour
Localised Pleural

Pleural dissemination

Malignant Effusion

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Parietal pleural / Chest wall Invasion
T4 extension into left atrium
Recurrent laryngeal nerve –left vocal cord palsy
Satellite nodules

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Asbestos exposure-folded lung
Synchronous lung primary
Synchronous lung and laryngeal

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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
    
    *KL Prenzel et al Chest. 2003;123:463–7*

- **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
    
    *YL Lv et al. Thorac Oncol. 2011;6:1350–8.*
Role of PET-CT: N Stage

- **Negative study:** Patients staged as N0 or N1 and M0
  - High NPV - true strength
  - Histological confirmation before surgical resection not needed
  - Avoids invasive mediastinoscopy
  - Valid only if primary FDG avid / absence of central tumour / hilar LN disease that may obscure coexisting N2 disease

- **Dual-time point imaging** can improve the sensitivity of FDG PET-CT for mediastinal nodal staging

- **Positive Study:** cannot be relied upon for accuracy
  - Low PPV
  - False positive: infection / inflammation

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
CT size significant but PET –ve node
# Role of PET-CT: N Stage

- Retrospective local audit

<table>
<thead>
<tr>
<th>PET/CT Report</th>
<th>Biopsy Positive (n 94)</th>
<th>Biopsy Negative (n 166)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>67</td>
<td>13</td>
</tr>
<tr>
<td>Negative</td>
<td>21*</td>
<td>119</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>6</td>
<td>34</td>
</tr>
</tbody>
</table>

- From reports: Sens 71%, Spec 71%, Acc 72%.
- SUV max > 3.0: Sens 85%, Spec 78%, Acc 79%.
- SUV max ratio > 0.20: Sens 82%, Spec 76%, Acc 78%.

*Stokes M, Hulse P, Kochhar R. SNM Annual Meeting 2012*
Role of PET-CT: N Stage

Results/ Recommendations of local audit

- Accuracy of PET/CT nodal staging in NSCLC could be improved using nodal SUVmax or SUVmax ratio, with optimum threshold values of 3 and 0.2 respectively.

- Improvement in test performance is insufficient to eliminate need for histological confirmation of N2/N3 nodes.

- A low rate of mediastinoscopy and biopsy for confirmation of PET-CT reported N2/N3 disease is being performed.

*Stokes M, Hulse P, Kochhar R. SNM Annual Meeting 2012*
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

Role of PET-CT: M Stage

Adrenal
• Masses in 20% - Adenoma vs metastases
• NCCT <10HU, SUV max >3.1, >2xhepatic uptake
• CT densitometry & Qualitative PET data
• Sens (100%) & Spec (99%)  

Bones
• Metastases - range 8% to 34%

<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>

Hepatic and Brain metastases - limitations
Adrenal metastasis
Unexpected bony metastasis
Role of PET-CT

Small Cell Lung Cancer

- Clinically more aggressive than NSCLC
- 60% to 70% extensive disease at presentation
- Data on SCLC with PET-CT limited
- Modification of stage & management in 10% to 33%
- Staging with PET-CT may separate favourable LS group

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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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
Other Clinical Uses & Advances of PET-CT

Prognostic Indicator

- Patients with a CMR significantly longer survival than PMR
  

- SUVmax of primary - independent prognostic factor for survival
  

Treatment Planning

- More accurately images tumour extent than CT alone
- Reduction of dose to normal surrounding tissue (PET tumour area <CT) & inclusion of adjacent viable tumour (PET tumor area > CT)
- Reduced inter and intra observer variability in planning
  
  Steenbakkers et al Int J Rad Oncol Biol Phys 2006 64: 435-448

Tracers Beyond FDG
PET CT & XRT Planning
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