Diagnostic Imaging Pathways - Non-Small Cell Lung Cancer (Staging)

Population Covered By The Guidance

This pathway provides guidance on imaging patients with confirmed non-small cell lung carcinoma on histology. This staging process will determine further definitive treatment.

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Quick User Guide

Move the mouse cursor over the PINK text boxes inside the flow chart to bring up a pop up box with salient points.
Clicking on the PINK text box will bring up the full text.
The relative radiation level (RRL) of each imaging investigation is displayed in the pop up box.

SYMBOL	RRL	EFFECTIVE DOSE RANGE
	None	0
	Minimal	< 1 millisieverts
	Low	1-5 mSv
	Medium	5-10 mSv
	High	>10 mSv

Pathway Diagram

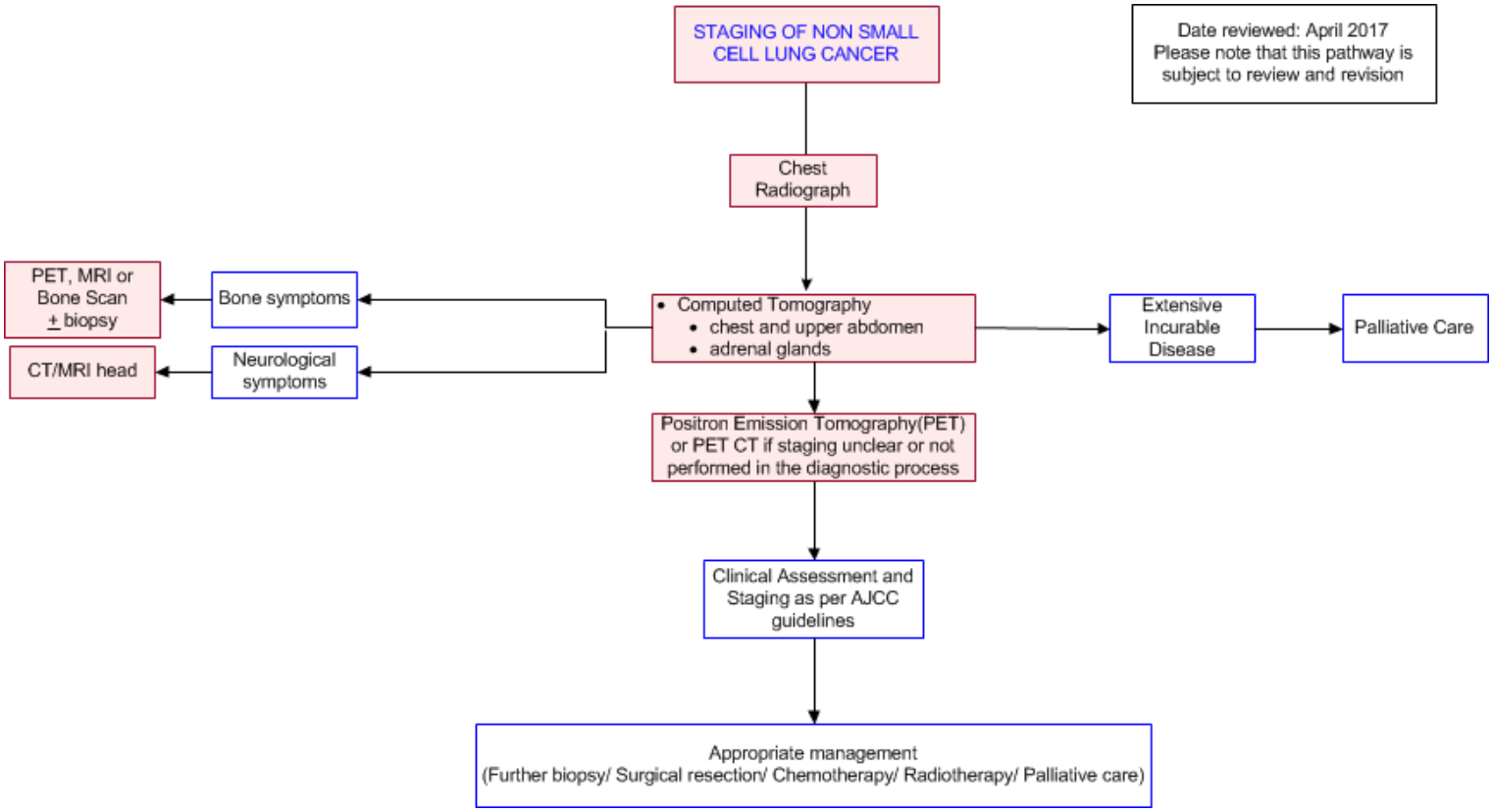
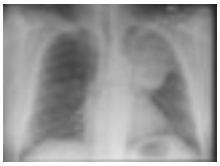


Image Gallery

Note: These images open in a new page

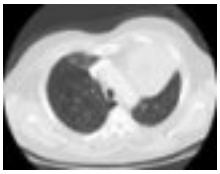
1a



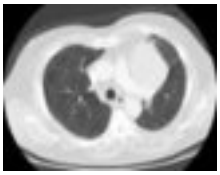
Lung Carcinoma

Image 1a (Chest radiograph: Left hilar mass causing collapse of the left upper lobe and elevation of the left main bronchus.

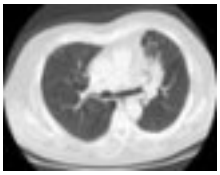
1b



1c



1d



Images 1b, 1c, and 2d (Computed Tomography): CT of the same patient reveals a large, relatively homogenous mass within the left upper lobe measuring 95mm and extending from the apex to the hilum. Central areas of low attenuation are compatible with tissue necrosis. There is also encasement of the left upper lobe bronchus and pulmonary artery with extensive background emphysema.

2a

Lung Carcinoma

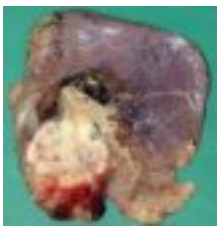


Image 2a: Lobectomy showing a large non-small cell lung carcinoma arising from the proximal bronchus and invading into the surrounding parenchyma. Note the patchy central necrosis and punctate areas of haemorrhage.

2b

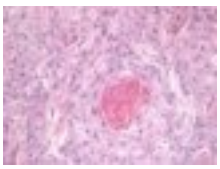
Images 2b and 2c: Post-mortem specimens showing infiltration of lung parenchyma by bronchoalveolar carcinoma.

2c

2d

Images 2d (H&E, x2.5) and 2e (H&E, x20): Histological sections of a moderately well differentiated squamous cell carcinoma of the lung showing infiltrating sheets and tongues of malignant squamous cells with whorls of keratin (blue arrows). At higher power, the malignant cells demonstrate marked nuclear atypia with abundant glassy eosinophilic cytoplasm.

2e



Teaching Points

- It is important to accurately stage NSCLC, as stages I to III are potentially resectable and in some instances curable. Accurately staging NSCLC can result in a higher quality of life in those with the disease as a result of more targeted and appropriate treatment
- Chest radiography is indicated in all patients but has low sensitivity for detecting lesion spread
- A CT of the chest and upper abdomen is indicated in all patients, as it allows for the evaluation of the size and extent of the primary tumour and metastatic spread to the mediastinum/upper abdomen
- A PET scan is indicated in all patients with NSCLC who DO NOT have evidence of stage IV (non-curative) disease on CT scans
- Increasingly, NSCLC is staged with combined PET-CT which is as accurate or superior to PET alone or CT alone
- Site specific symptoms warrant directed evaluation of that site with the most appropriate study
- Palliative care for NSCLC may include non-curative chemotherapy, radiation and/or surgery

Staging Of Non-Small Cell Lung Cancer (NSCLC)

- Precise staging is essential for therapeutic decision making and prognostic information 1-3
- TNM classification is the preferred system of staging 2, 4, 5
- Important to accurately differentiate stages I to IIIA (potentially resectable) from stage IIIB to IV (non-resectable) cancer 6, 7

TNM Staging of Non-Small Cell Lung Cancer 8

T: Primary Tumour		
Tx	Primary tumour cannot be assessed or tumour proven by presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy	
T0	No evidence of primary tumour	
Tis	Carcinoma in situ	
T1	Tumour ?3 cm in greatest dimension surrounded by lung or visceral pleura without bronchoscopic evidence of invasion more proximal than the lobar bronchus (ie, not in the main bronchus)	
T1a(mi)	Minimally invasive adenocarcinoma	
T1a	Tumour ?1 cm in greatest dimension	
T1b	Tumour >1 cm but ?2 cm in greatest dimension	
T1c	Tumour >2 cm but ?3 cm in greatest dimension	
T2	Tumour >3 cm but ?5 cm or tumour with any of the following features • Involves main bronchus regardless of distance from the carina but without involvement of the carina • Invades visceral pleura • Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part	

	or all of the lung
T2a	Tumour >3 cm but ?4 cm in greatest dimension
T2b	Tumour >4 cm but ?5 cm in greatest dimension
T3	Tumour >5 cm but ?7 cm in greatest dimension or associated with separate tumour nodule(s) in the same lobe as the primary tumour or directly invades any of the following structures: chest wall (including the parietal pleura and superior sulcus tumours), phrenic nerve, parietal pericardium
T4	Tumour >7 cm in greatest dimension or associated with separate tumour nodule(s) in a different ipsilateral lobe than that of the primary tumour or invades any of the following structures: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, and carina
N: Regional lymph node involvement	
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)
M: Distant metastasis	
M0	No distant metastasis
M1	Distant metastasis present
M1	Separate tumour nodule(s) in

a	a contralateral lobe; tumour with pleural or pericardial nodule(s) or malignant pleural or pericardial effusion
M1b	Single extrathoracic metastasis
M1c	Multiple extrathoracic metastases in one or more organs

Stage groupings	T	N	M
Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	T1a(mi)	N0	M0
	T1a	N0	M0
Stage IA2	T1b	N0	M0
Stage IA3	T1c	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
Stage IIB	T1a to c	N1	M0
	T2a	N1	M0
	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a to c	N2	M0
	T2a to b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a to c	N3	M0
	T2a to b	N3	M0
	T3	N2	M0
	T4	N2	M0
Stage IIIC	T3	N3	M0
	T4	N3	M0
Stage IVA	Any T	Any N	M1a
	Any T	Any N3	M1b
Stage IVB	Any T	Any N	M1c

Plain Chest Radiography (CXR)

- Routinely indicated in patients with lung cancer 6
- Readily available, inexpensive, and minimal effective radiation dose 9
- Limitations - lacks sensitivity in the detection of mediastinal lymph node metastases, and in chest wall and mediastinal invasion 10

Computed Tomography (CT)

Chest, Upper Abdomen

- For patients with either a known or suspected lung cancer who are eligible for treatment, CT scan of the chest with contrast is recommended 11
- The usual CT protocol for NSCLC involves a CT chest with extension into the upper abdomen (adrenals). This allows for evaluation of the size and extent of the primary tumour, and metastatic spread to mediastinum and upper abdomen (particularly liver, adrenal glands) 6, 11
- IV contrast may be administered to help distinguish vascular structures from centrally located tumours & lymph nodes
- Limitations
    - CT has only moderate T staging accuracy. The positive predictive value (PPV) of CT for T3 or T4 disease is only 68% and as such, a positive result should be confirmed histologically before denying patients curative surgery (unless there is overt evidence of non-resectable disease such as bony destruction or vascular invasion) 3, 12, 13
    - CT has low accuracy in the identification of mediastinal metastases compared to PET with a median sensitivity and specificity of 61% and 79% respectively. Thus CT is not a reliable modality for staging the mediastinum in patients with NSCLC 14
    - Although the accuracy of CT in detecting malignant lymph nodes is only about 67%, it provides good anatomic information and can guide the choice of lymph nodes for further invasive biopsy 14, 15
    - CT has limited ability to evaluate superior sulcus tumours due to its axial format and streak artefacts from the shoulders. MRI may be of benefit in this circumstance 3, 13
    - The relatively low sensitivity and specificity of CT (55 and 81 percent) and PET (80 and 88 percent) can miss occult cancer (false negatives) 11, 16
- More recently, CT has been integrated with PET (PET-CT) to provide combined functional & anatomical imaging in the same sitting 3

Adrenal Glands

- CT is the primary imaging modality for characterisation of adrenal masses. 11, 17 While the majority of adrenal lesions are benign, the risk of malignancy increases with primary tumour stage & the size of the adrenal lesion. Lesions >5cm in size are likely to be malignant and these patients should be referred for surgery 17-19
    1. Lesions of 20 HU are likely malignant and should be biopsied when the result influences management
    2. CT indeterminate lesions (11-20 HU) can be further characterised by MRI, PET, PET-CT or by using CT washout criteria 21
- When the adrenal lesion is the sole potential site of metastatic disease, biopsy & histopathological confirmation should be sought 19, 20, 23, 24

Positron Emission Tomography (PET)

- PET utilises a radioactive glucose-analogue (18-FDG) to image tissues that preferentially uptake glucose. Non-small cell lung cancer tumours have a very high affinity for glucose and readily take up 18-FDG 7, 25
- PET is able to accurately detect unsuspected distant metastases in 15% of surgical candidates and changes management in 25% of patients 7, 11, 26
- PET is superior to CT in differentiating resectable from non-resectable disease 12, 14, 25
- PET is indicated in all patients with non-small cell lung cancer unless CT scan unequivocally shows overwhelming radiographic evidence of metastatic disease in multiple sites 11
- If PET is unavailable, bone scan and abdominal CT are reasonable alternatives to evaluate for

extra thoracic disease 7, 11

- Advantages
  - Superior to CT for nodal staging of non-small cell lung cancer 12, 14, 23, 24, 27
  - Superior to CT and bone scan for detection of distant metastases 7, 25
- Cost-effective in reducing the number of unnecessary thoracotomies 25, 27, 28
- Disadvantages
  - Relatively poor resolution to assess tumour size and determine invasion into adjacent tissues, such as chest wall, large vessels, or other features that define tumour status 27, 29, 30
  - Low sensitivity for detection of brain metastases 11, 27
  - Moderate positive predictive value (79%) for diagnosis of mediastinal lymph node metastases, thus histological confirmation of PET positive nodes has been recommended 25, 29, 31
- There is no need for curative surgical resection in Stage IV because of distant metastasis. An important advantage of PET-CT is the use of whole-body scanning to detect distant metastasis 25

PET-CT

- The role of PET-CT in the management of non-small cell lung cancer continues to emerge with time. 32 Despite its increasing use, there is no consensus regarding the routine use of integrated PET/CT as a staging modality for patients with suspected NSCLC 33
- The limited evidence so far indicates that PET-CT is as accurate or superior to PET alone. 23, 26, 31, 34
- PET-CT has a good sensitivity & specificity for nodal staging (84%, 89% respectively), and for staging distant metastases (93%, 96% respectively). If this technique is not available, visual correlation of PET and CT can be a valuable alternative 3, 35
- Limitations
  - Sensitivity for brain metastases is limited (60%) 11, 23
  - Limited availability and high expense 3, 36
  - Due to technological limitations of PET/CT, lesions that measure less than two to three times the spatial resolution of the scanner will usually appear less active due to the partial volume effect 13
- The limited evidence suggests that PET/CT represents the best non-invasive modality for the detection of nodal metastasis, although mediastinoscopy is still required whenever there is uncertainty regarding the status of any one lymph node in patients with NSCLC 3

Bone Scan or Magnetic Resonance Imaging (MRI)

- Site specific symptoms warrant directed evaluation of that site with the most appropriate study 11
- Routine skeletal imaging is usually not indicated 37
- Some studies have indicated that bone scintigraphy following PET is of limited use as PET is more sensitive and specific in detecting bone metastases secondary to NSCLC. Some authors have recommended use of MRI when an abnormality on PET has been detected 38-40

Computed Tomography (CT) / Magnetic Resonance Imaging (MRI) Head

- Routine use of brain imaging in asymptomatic patients with NSCLC is not indicated and should be limited to patients with symptoms or in those who are more likely to have metastatic disease 41

- Clinical examination is useful for ruling out cerebral metastases with a negative predictive value of 94% 14, 24, 42
- CT may be the preferred initial investigation for cerebral metastases, but MRI has higher sensitivity. 23 CT and MRI are more effective than PET for assessing cerebral metastases due to high physiological glucose uptake in the brain 23, 41

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Date of literature search: January 2017

References are graded from Level I to V according to the Oxford Centre for Evidence-Based Medicine, Levels of Evidence. Download the document

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