East Midlands Strategic Clinical Networks

East Midlands Lung & Mesothelioma Expert Clinical Advisory Group (ECAG)

Guidelines for the Investigation and Treatment of Lung Cancer

Version 4.0

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Contents

1. Introduction

Lung cancer is the most common cause of death from malignant disease in the UK. Previous reports have highlighted marked variation in the management of patients with lung cancer and the need for clear guidelines regarding standards of care for these patients.

These clinical guidelines represent the East Midlands Network adoption and adaptation of the available national clinical guidelines. These include the updated NICE Guideline on the management of lung cancer, CG121, http://guidance.nice.org.uk/CG121 the NICE guidelines on referral for suspected cancer CG27, http://www.nice.org.uk/search?q=referral+for+suspected+cancer and the NICE guideline on palliative care, http://www.nice.org.uk/search?q=palliative+care+guideline.

Reference is also made to the British Thoracic Society (BTS) Guideline for the radical management of lung cancer https://www.brit-thoracic.org.uk/document-library/clinical-information/lung-cancer/lung-cancer-guidelines/btsscts-guidelines-on-the-radical-management-of-patients-with-lung-cancer/ and the BTS guidelines for standard bronchoscopy, https://www.brit-thoracic.org.uk/document-library/clinical-information/bronchoscopy/flexible-bronchoscopy/diagnostic-flexible-bronchoscopy-in-adults-guideline-2013/ and advanced bronchoscopy, https://www.brit-thoracic.org.uk/document-library/clinical-information/bronchoscopy/advanced-diagnostic-and-therapeutic-bronchoscopy/bts-advanced-bronchoscopy-guideline/

2. Scope of guidelines

All Trusts within the East Midlands Clinical Network are expected to follow this guideline. The Trusts within the East Midlands Clinical Network are:

- Burton Hospitals NHS Foundation Trust (BHFT)
- Derby Hospitals NHS Foundation Trust (RDH)
- Kettering General Hospital NHS Foundation Trust (KGH)
- Northampton General Hospital NHS Trust (NGH)
- Nottingham University Hospitals (NUH)
- Sherwood Forest Hospitals NHS Foundation Trust (SFHT)
- United Lincolnshire Hospitals NHS Trust (ULHT)
- University Hospitals of Leicester NHS Trust (UHLT)

This guideline is relevant to:

- Adults (18 years and older) with newly diagnosed non-small-cell lung cancer (NSCLC)
- Adults with newly diagnosed small-cell lung cancer (SCLC)
- Adults with relapsed NSCLC
- Adults with relapsed SCLC

- Adults with mesothelioma

This guideline does not cover:

- Adults with lung metastases arising from primary cancers originating outside the lung
- Children (younger than 18) with lung cancer.
- Rare lung tumours (for example, pulmonary blastoma)
- Benign lung tumours (for example, bronchial adenoma)
- Carcinoid (typical or atypical)

3. Access to services and referral

3.1 GP Presentation and Urgent 2 Week Wait Referrals

Most referrals will be made from the GP to the lung cancer team, but these guidelines also cover other types of referral e.g. consultant-to-consultant. In those situations where a non-urgent referral is made, the responsible clinician will ensure that the referral receives the appropriate urgency.

From NICE CG27:
Consider immediate referral for patients with:

- signs of superior vena caval obstruction (swelling of the face/neck with fixed elevation of jugular venous pressure)
- stridor

Refer urgently for chest X-ray (the report should be returned within 5 days) for patients with any of the following:

- Haemoptysis
- unexplained or persistent (longer than 3 weeks):
    - chest and/or shoulder pain
    - dyspnoea
    - weight loss
    - chest signs
    - hoarseness
    - finger clubbing
    - cervical or supraclavicular lymphadenopathy
    - cough
    - features suggestive of metastasis from a lung cancer (for example, in brain, bone, liver, and skin)
    - underlying chronic respiratory problems with unexplained changes in existing symptoms
    -

Refer urgently patients with:

- persistent haemoptysis (in smokers or ex-smokers aged 40 years and older)
- a chest X-ray suggestive of lung cancer (including pleural effusion and slowly resolving consolidation)
- a normal chest X-ray where there is a high suspicion of lung cancer
- a history of asbestos exposure and recent onset of chest pain, shortness of breath or unexplained systemic symptoms where a chest X-ray indicates pleural effusion, pleural mass or any suspicious lung pathology.

The following patients have a high risk of developing lung cancer. An urgent referral for a chest X-ray or to a specialist can be considered sooner in these patients (for example, if signs and symptoms have lasted less than 3 weeks):

- all current or ex-smokers
- patients with chronic obstructive pulmonary disease
- people who have been exposed to asbestos
- people with a previous history of cancer (especially head and neck)

The patient will be telephoned within 2 working days of receipt of the urgent referral and offered an out-patient appointment. The patient will be seen for their 1st OP appointment within 14 days of referral. A CT scan may be organised by the lung cancer MDT prior to the initial OPA – the patient should be informed of this by the secondary care team and the GP should also indicate to the patient that this might happen.

It is the responsibility of the referrer to inform the patient about the result of their chest x-ray and the details of the referral to the chest physician.

3.2 First Out-Patient Appointment

At the first out-patient appointment a full history and examination will be carried out. A full history and examination includes:-

- Smoking history
- Occupational history
- Palpation of supraclavicular nodes and liver

Further investigations will normally be carried out – these may include:-

- CT scan thorax and upper abdomen including the lower neck, liver and adrenals (if not already done)
- Spirometry
- Blood investigations (FBC, U+Es, LFTs and calcium)
- Other investigations as clinically indicated according to the findings on the CT scan and guided by the NICE GL 121 diagnosis and staging algorithm

4. Diagnosis and staging

4.1 Bronchoscopy

A bronchoscopy patient information leaflet is given following explanation of procedure at the first out-patient appointment. The patient will normally undergo a bronchoscopy within 7 days of their first OP appointment.

Bronchoscopy patients should be treated as day cases unless there are specific reasons for inpatient care. All patients undergoing bronchoscopy should be assessed beforehand by a member of the medical team. Informed consent should be taken according to the local Trust policy.

British Thoracic Society Guidelines (2013 update) should be followed. This is available at the following link: https://www.brit-thoracic.org.uk/document-library/clinical-information/bronchoscopy/flexible-bronchoscopy/diagnostic-flexible-bronchoscopy-in-adults-guideline-2013/

The guideline includes sections on:

- Bronchoscopy in respect of comorbidities such as asthma and ischaemic heart disease
- Routine pre-procedure care including fitness, anticoagulant therapy and food and liquid ingestion.
- Intravenous access and safe sedation
- Monitoring and oxygen therapy
- Standards for biopsy, brush, wash and lavage samples
- Minimum diagnostic standards and audit

The bronchoscopy findings should be documented in the patient's health record. The result of the histology and cytology should be available within 7 days of the procedure.

4.2 Endobronchial Ultrasound

Endobronchial Ultrasound (EBUS) is an endoscopic technique for sampling mediastinal and hilar lymph nodes. EBUS is available in Nottingham, Derby, Sherwood Forest, Leicester and Northampton. Local referral guidelines and pathways are in place for patients to be referred from outlying MDTs.

The BTS guidelines on advanced bronchoscopy provide detailed guidance.

5. Imaging guidelines

Radiology is a key part in the management of lung cancer. The East Midlands Clinical Network Guidelines are based predominantly on the NICE Guidelines, Royal College of Radiologists Guidance and evidence based local practice.

5.1 Staging CT

Patients with known or suspected lung cancer should be offered a contrast-enhanced chest CT scan (if suitable renal function and no significant contrast allergy) to further the diagnosis and stage the disease. The scan should also include the liver and adrenals.

Chest CT should ideally be performed early in the patient journey prior to invasive procedures such as bronchoscopy, percutaneous biopsy, pleural drainage or other biopsy procedure.

In the assessment of chest wall or mediastinal invasion, CT alone may be unreliable and other imaging techniques should be considered.

5.2 MRI

For patients with either known or suspected lung cancer who are eligible for treatment, MRI of the chest should not be performed routinely for staging the mediastinum. MRI may be useful in patients with NSCLC where there is concern for involvement of the superior sulcus or brachial plexus involvement.

Staging investigations should be no older than 6 weeks when being used to make management decisions.

5.3 PET Scanning

PET has an established role in the staging of non-small cell lung cancer and in the evaluation of solitary pulmonary nodules. In general terms, the following may be considered as the key clinical indications for PET (Inter-Collegiate Standing Committee on Nuclear Medicine 2003 and NICE Guidelines 2005):-

- Differentiation of benign versus malignant lesions if the initial investigations are inconclusive or if there is contradiction to biopsy
- Staging of non-small cell lung cancer where there is radical treatment intent
- Assessment of recurrent disease in previously treated areas if other imaging is inconclusive.

Where PET scan requests are discussed with the PCT with regards to funding this must be done promptly with no delay to the patient pathway.

CT-PET should be performed on all patients with confirmed or suspected NSCLC prior to radical treatment. However, PET scanning may be considered inappropriate where other staging investigations (in particular CT) suggests stage I disease – in these patients, the yield of unsuspected N2 or M1 disease is low.

Mediastinal sampling should not routinely be performed if there is no significant CT-PET nodal uptake in patients who are otherwise suitable for radical treatment.

Histological/cytological investigation should be performed to confirm N2/3 disease where FDG-PET is positive unless there is definite distant metastatic disease or where there is a high probability that the N2/N3 disease is metastatic (for example, if there is a chain of high FDG uptake in lymph nodes). When a PET scan for N2/N3 disease is negative, biopsy is not required where the nodes measure <10mm short axis but is still recommended for larger nodes due to the false negative rate of PET in larger nodes. Histological/cytological investigation should be performed to confirm N2/3 disease where FDG-PET is positive. This should be undertaken by the most appropriate method.

The role of PET in mesothelioma and small cell lung cancer is not yet established. It may be undertaken as part of a clinical trial or on an individual problem solving basis after discussion in the MDT and with a specialist radiologist.

5.4 Ultrasound

There should be a readily available U/S service for the evaluation of patients with suspected occult supra clavicular nodes and to guide pleural aspiration and drainage. This should be performed before more invasive mediastinal sampling particularly if supra clavicular nodes are detected on CT.

5.5 Brain Imaging

Contrast enhanced CT or MRI should be performed in patients with clinically suspected brain metastases.

Routine brain imaging is not recommended in asymptomatic patients prior to radical surgery with suspected stage I and II NSCLC or with SCLC.

Contrast enhanced MRI of the brain may be performed in all patients being considered for radical multi-modality treatment for stage IIIa/b disease NSCLC.

5.6 Biopsy

Units should have appropriate radiologists capable of performing lung parenchymal and pleural biopsy. Image-guided lung biopsies should be carried out according to BTS guidelines.

Plus:

- At least five bronchial biopsy specimens should be taken in cases of suspected bronchial malignancy
- Biopsies, brushings and washings should all be obtained in cases of suspected endobronchial malignancy
- A minimum diagnostic level of at least 80% should be obtained from a combination of biopsies, brushings, and washings in cases of endoscopically visible malignancy

The bronchoscopy findings should be documented in the patient's health record. The result of the histology and cytology should be available within 7 days of the procedure.

5.7 Organisational Issues

Patients with a new/unexpected diagnosis of suspected lung cancer or other thoracic malignancy on chest x-ray or CT should have a copy of this report sent to the lung cancer (or 2WW) team.

Lung MDTs should have a designated lead Radiologist(s) with appropriate allocated time in their job plans.

All MDTs should have a radiologist available to them with adequate viewing and projection facilities. Full text reports of imaging from other units should be sent with the imaging.

All available historic images should be available and viewed at the time of diagnosis. Cases should be reviewed by designated radiologists at and also ideally prior to the lung MDT.

Imaging from referring centres and CT-PET images should be available and ideally loaded on to PACS at the time of treatment.

Contemporary imaging should be available prior to the MDT making management decisions or the patient undergoing radical treatment. CT should be < 6 weeks old (or < 4 weeks if borderline central tumours). CT PET should be < 8 weeks old.

Patients with imaging studies consistent with distant metastases should not be excluded from potentially curative treatment without tissue confirmation or overwhelming clinical and radiographic evidence of metastases.

5.8 Evaluation of a Solitary Pulmonary Nodule (SPN)

As there are no national guidelines on this subject, local arrangements will apply. However, it is recommended that organisations have a clear policy in place.

5.9 Staging

Traditionally, non-small cell cancers are staged using the TNM system. Small cell tumours are often staged as limited disease or extensive disease, but the TNM system is now recommended for these tumours. From January 2010 all new patients will be staged using the 7th UICC Staging Classification.

Most patients do not undergo surgery; therefore staging is determined radiologically and clinically. CT scanning is the main radiological staging investigation, supplemented where appropriate by PET scanning. This may be supplemented by ultrasound of the liver where LFTs are abnormal, or by bone scanning if calcium/Alkaline Phosphate is raised or there is bony pain. If the patient has neurological symptoms consider MRI or CT Brain.

6. Pathology guidelines

Pathology samples will be dealt with according to the principles described in current national guidelines and RCPath documentation: RCPath standards and datasets for reporting cancers: Dataset for lung cancer histopathology reports, 3rd edition, April 2011,G048; Tissue Pathways for non neoplastic thoracic pathology 2013, G135; Dataset for the histological reporting of Mesothelioma 2013, G134; Quality Assurance in Histopathology and Cytopathology Reporting Practice 2009, and the individual laboratory's documented procedures.

Histological type is classified according to WHO typing of lung tumours (2004) along with the modifications to adenocarcinoma classification described in the IASLC/ATS/ERS classification of adenocarcinomas 2011 (Travis et al, J Thoracic Oncol, 2011:6,244-85).

Molecular testing* of biopsy histology or cytology samples from patients with a diagnosis of non small cell non squamous lung carcinoma should be carried out unless treatment is not considered (e.g. patients >85 years old – this will be a local decision).

Any samples that come from diagnostic tests e.g. lymph nodes, pleura, endobronchial, transbronchial biopsies, EBUS – TBNA etc. can be sent for molecular testing directly once it has been determined that the samples are from a non squamous non small cell lung cancer. However, immunocytochemistry should not be done routinely on small biopsies unless there is a serious likelihood the carcinoma is not a lung primary; as much tissue as possible needs to remain available for molecular analysis.

Molecular testing is not currently routinely recommended on surgical resections.

Testing may be carried out on either histological or cytological material. Individual laboratories will develop their own arrangements and protocols for this which may involve samples being sent away to a referral laboratory if the test is not performed in house.

The testing laboratory should participate in a recognised quality assessment scheme , e.g. UK NEQAS. The tests used for analysis should comply with current NICE guidelines. (Aug 2013 – recommendations for EGFR-1 testing).

* Currently (2013) comprises EGFR-1, ALK, KRAS

All malignant pleural biopsies will be subjected to immunohistochemistry in order to differentiate mesothelioma from metastatic carcinoma or other tumours where appropriate.

7. Multidisciplinary team

All patients with a working diagnosis of lung cancer should be discussed in a lung cancer multidisciplinary meeting. Local arrangements will determine how patients are entered onto the meeting agenda. The meetings take place weekly where members discuss the management of patients before plans are agreed.

Members of the lung team should include medical and nursing staff with specialized knowledge of diagnosis and treatment, both curative and palliative of lung cancer.

The team will be led by a lead clinician and may work in more than one hospital site.

Core team members:

- Respiratory physician – with special interest in lung cancer
- Radiologist – with thoracic expertise
- Pathologist +/- cytologist
- Clinical Nurse Specialist (CNS)
- Oncologist
- Palliative Care Physician
- Palliative Care CNS
- Thoracic Surgeon
- MDT Coordinator / secretary

In addition the team should have close links with:

- Psychologist/psychiatrist
- NCRN team member
- Social worker
- Chaplain/pastoral care worker
- Bereavement care worker
- Primary health care teams

All decisions should be recorded and communicated to the patient and their GP. The decision should also be entered into the patients' permanent health record.

7.1 Lung Cancer Clinical Nurse Specialists

In accordance with NICE guidelines, all patients with suspected lung cancer/mesothelioma should have access to a lung cancer specialist nurse (key worker). The lung cancer CNS should meet all patients pre-diagnosis and provide specialist advice/information to all patients and carers throughout the diagnostic and treatment pathway. The lung cancer CNS will undertake a specialist holistic assessment of needs. This will include symptom control, financial assessment, co-ordination of the patient pathway and the development of ongoing therapeutic relationships. The lung cancer CNS should provide appropriate support through survivorship and palliative care.

8. Communicating the diagnosis

The patient should be told their diagnosis and treatment options in a calm and sensitive manner, where possible in the presence of a specialist nurse. They should be offered a permanent record of the discussion and should be offered written (or other) information relevant to their circumstances. They should also be offered the name and contact details of a key worker, who will normally be the specialist nurse.

A checklist in the patient's notes should confirm that these have been offered.

Following the communication of the diagnosis to the patient, the patients' GP will be informed of the diagnosis and treatment plan within 24 hours.

9. Data collection

The local teams are responsible for data collection. The network has agreed to adopt the National Lung Cancer Audit (NLCA) minimum dataset. Local arrangements will apply for the collection and uploading of data to the database. Audit of outcomes and action that may be stimulated by audit findings should be discussed in team meetings.

10. Referral to surgical centre

Local arrangements for surgical referral exist in each organisation, but the following principles should be applied:

- Patients with NSCLC (stage 0 up to IIIA) should be considered for surgery.
- Surgery in patients with IIIA (N2) NSCLC detected through pre-operative staging is associated with a relatively poor prognosis, and such cases should be considered carefully by the lung cancer MDT. Single station N2 disease should be considered for surgery.
- Patients with oligometastatic disease may be suitable for thoracic surgery and metastectomy.
- Guidelines regarding fitness for surgery exist (updated BTS Guidelines published 2010) but should not prevent individual assessment by a thoracic surgeon.

Elective surgery should only be undertaken after adequate diagnosis and staging, in order to minimize the number of inappropriate thoracotomies. Local arrangements for assessing fitness for surgery will apply. Open-and-close thoracotomies should be no more than 2%.

Because of the morbidity and mortality associated with surgery, it is important that patients are given realistic information about both the risks and benefits.

Patients with mesothelioma may benefit from radical or palliative surgery – it is especially important that these cases are discussed in a multidisciplinary setting (which will usually be a specialist mesothelioma MDT) and in the light of currently available clinical trials.

11. Treatment of NSCLC

11.1 Surgery

- Patients with NSCLC (stage 0 up to IIIA) should be considered for surgery.
- Surgery in patients with IIIA (N2) NSCLC detected through pre-operative staging is associated with a relatively poor prognosis, and such cases should be considered carefully by the lung cancer MDT.
- Patients with oligometastatic disease may be suitable for thoracic surgery and metastectomy.

11.1.1 Down-Staging Chemotherapy/Radiotherapy

Carefully selected patients may be considered for surgery after the completion of their initial chemotherapy/radiotherapy. These patients need to be restaged by PET-CT, and possibly also by MRI of the brain if they still appear to be suitable.

11.1.2 Adjuvant Chemotherapy

See section on Oncological Management.

11.2 Radiotherapy

11.2.1 Radical Radiotherapy

If FEV1 is satisfactory and disease volume is reasonable, radical RT should be offered to patients who do not undergo surgery. Concurrent chemo-radiotherapy may be preferred in selected patients depending upon local facilities and experience. Similarly, radical radiotherapy may be offered after induction chemotherapy in selected cases. CHART radiotherapy is the preferred treatment in appropriate cases. In all situations, potential benefits must be balanced against the risk of adverse effects and discussed with the patient.

Stereotactic ablative radiotherapy (SABR) has been commissioned for the East Midlands via NUH and UHL. Patients with a primary peripheral tumour <5cm and no nodes or metastases should be considered for SABR and if in doubt referred to the Lung cancer oncologists at NUH or UHL for assessment. Patients need to be WHO PS 0-2 but there is no minimum lung function. Pathological confirmation is desirable but not essential if the tumour is growing on CT scans and PET positive.

11.2.2 Post-Operative Radiotherapy

Should be considered following incomplete resection with the aim of improving local control.

11.2.2.1 Palliative Radiotherapy (including brachytherapy)

This is effective in symptom control, especially:

- Haemoptysis
- Chest pain
- Possibly cough and breathlessness
- Impending obstruction
- Recurrent infections

High dose palliative RT could be considered in appropriate patients.

11.2.2.2 Cranial Irradiation for Brain Metastases

Whole brain radiotherapy remains the standard option for patients with brain metastases, in order to improve symptoms. However, there is little evidence to support the practice and the effect on quality of life is unknown. Where possible, the patient should have the opportunity to enter a clinical trial of WBRT.

Patients with solitary brain metastases on MRI should be considered for surgical resection or stereotactic radiosurgery.

11.3. Chemotherapy

i) Chemotherapy should only be given in a designated day case area with close supervision of chemotherapy specialist nurses and oncologists in accordance with JCCO guidelines. There should also be expert pharmacy and 24-hour laboratory support.

ii) Adjuvant chemotherapy should be offered to pathological stage T1-3N1-2M0 resections who have recovered from surgery and maintained a good PS of 0-2. Patients with pathological stage T2-3N0M0 tumours >4cm in diameter may also be considered after full discussion of the relative risks and benefits.

iii) Down-staging chemotherapy +/- surgery/RT would be appropriate in select Stage III A/B patents.

iv) Chemotherapy should be offered to patients with stage III or IV NSCLC and good performance status (0, 1 and possibly 2), to improve survival, disease control and quality of life.

v) Patients with EGFR mutations should be offered a TKI as first line treatment.

11.3.1 Chemotherapy Regimens

Chemotherapy for advanced NSCLC should be a combination of a single third generation drug plus a platinum drug. The exact regime will depend on local preference and experience. Single agent chemotherapy may be a suitable choice for appropriate patients who are unfit for a platinum regime.

Second-line treatment should be considered in patients with locally advanced or metastatic NSCLC in whom relapse has occurred after previous chemotherapy. Such patients should be selected on an individual basis.

The chemotherapy algorithms are included on the EMCN website:-

http://www.eastmidlandscancernetwork.nhs.uk/_HealthProfessionals-Chemotherapy-Oncology-LungCancer.aspx

11.4 Other Treatment Modalities for NSCLC

11.4.1 Photodynamic therapy

Patients with endobronchial tumour unsuitable for any other treatment modality may be considered for PDT. Patients with carcinoma in situe and pre-malignant lesions may also be considered for PDT. There is currently no provision for PDT in East Midlands Cancer Network and, therefore, patients must be referred out of region.

11.4.2 Radiofrequency Ablation (RFA)

RFA may be considered for lung primary lesions <3cm in diameter (or single or multiple lung metastases <3cm in diameter) that are unsuitable for resection. RFA is currently being offered by Nottingham City Hospital and can be accessed by referring to Prof David Baldwin.

12. Treatment of small cell lung cancer (SCLC)

12.1 Surgery

Surgery should be considered for T1-3N0-1M0 SCLC followed by multimodality treatment.

12.2 Chemotherapy

Chemotherapy is the main modality of treatment and should be offered to all patients who are fit enough to receive treatment. Platinum based chemotherapy, especially multi-drug regimes, is more effective than single agent regimes. Benefits vs side effects and morbidity should be carefully balanced.

Four to six cycles of chemotherapy should be considered and offered to fit patients with responding disease. Maintenance treatment is not recommended. Second-line chemotherapy should be offered to patients at relapse if appropriate.

The chemotherapy algorithms are included on the EMCN website:-

http://www.eastmidlandscancernetwork.nhs.uk/_HealthProfessionals-Chemotherapy-Oncology-LungCancer.aspx

12.3 Radiotherapy

Patients with limited stage disease should be considered for consolidation thoracic radiotherapy following chemotherapy or concurrent chemo-radiotherapy where appropriate.

For patients with poor performance status palliative radiotherapy to chest and metastatic disease are reasonable options for symptomatic relief if survival is expected to be more than 4 weeks.

12.4 Prophylactic Cranial Irradiation (PCI)

Both limited and extensive stage patients under 75 years of age who have a good response to primary chemotherapy should be considered for PCI.

13. Palliative interventions and care

13.1 Symptom Management

The majority of lung cancer patients present with relatively advanced disease. For these patients, symptom control and palliation are central to their management plans.

Common symptoms are:

- Pain
- Breathlessness
- Cough
- Weakness

13.2 Referral to Palliative Care Team

Local arrangements will apply, but clear referral pathways should be in place to allow prompt assessment and treatment by the palliative care team.

13.3 Palliation of Specific Symptoms

The table below lists strategies recommended by NICE. Local arrangements will apply.

Symptom	Management
Breathlessness	• External beam radiotherapy • Non-drug interventions (psychosocial support, breathing control and coping strategies) Intrinsic airway obstruction • De-bulking bronchoscopic procedures • Endobronchial therapy (e.g. brachytherapy) for endobronchial symptoms not palliated by other means Extrinsic airway compression • Stents Pleural effusion • Pleural aspiration/drainage for pleural effusion • Talc pleurodesis if symptoms improve after aspiration/drainage of fluid
Cough	• External beam radiotherapy
Haemoptysis	• External beam radiotherapy
Chest pain	• External beam radiotherapy
Hoarseness	• Referral to ear, nose and throat specialist
SVC obstruction	• Chemotherapy and radiotherapy, depending on stage of disease and performance status • Stent insertion for immediate relief of severe symptoms or after failure of earlier treatment
Symptoms from brain metastases	• Corticosteroids and radiotherapy
Spinal cord compression	• Corticosteroids, radiotherapy and surgery where appropriate, within 24 hours • Early referral to oncology physiotherapist and occupational therapist.
Symptoms from bone metastases	• Single-fraction radiotherapy if standard analgesic treatments are inadequate.
Other symptoms	• Management by multidisciplinary groups including supportive and palliative care professionals should address other symptoms, including weight loss, loss of appetite, difficulty swallowing, and depression.

13.4 Guidelines for Palliative Care in Mesothelioma

13.4.1 Supportive and palliative care

Supportive and palliative care of patients with mesothelioma and their families is very important, given that the disease has a poor and relatively well-defined prognosis and that most patients need symptom palliation from the time of diagnosis onwards.

Management of pain and other symptoms and provision of psychological, social and spiritual support is paramount. The goal is achievement of the best quality of life for patients and their families. Referral of the patient and/or their carers to specialist palliative care services is appropriate for a range of issues. These include unresolved symptoms and complex physical, psychological or spiritual needs, and end-of-life and bereavement issues.

13.4.2 Symptom Control

All symptoms need a working diagnosis, as some may be caused by concurrent non-cancer related problems. It is often helpful to record symptom severity on a simple scale to assess progress and response to treatment. Relief of pain, breathlessness and other symptoms can occur with response to chemotherapy.

13.4.3 Dyspnoea

The common causes of breathlessness in mesothelioma are pleural effusion, lung compression and chest wall stiffness. Weakness and malaise, and anxiety or panic will be treated according to general palliative care guidelines that include pharmacological approaches such as opioids, benzodiazeines and oxygen and non-pharmacological methods such as breathing exercises and relaxation combined with re-adaptation.

Cough, anorexia, weight loss, fatigue, excessive sweating and depression all occur in malignant mesothelioma and should be managed according to palliative care guidelines.

13.4.4 Recurrent Effusions

In patients with poor prognosis, symptomatic pleural aspiration is appropriate. Insertions of a tunnelled pleural catheter is the preferred method for controlling recurrent and symptomatic malignant effusions including patients with trapped lung with a prognosis of more than 4 weeks. Surgical pleurectomy is an alternative option for selected patients.

13.4.5 Pain

The treatment of pain in malignant mesothelioma follows the same principles as for any other cancer but can include more specific techniques where initial methods are inadequate. These may necessitate early referral to a specialist pain service.

Specific techniques include:-

- Transcutaneous electrical nerve stimulation machines and acupuncture.
- Intercostal, paravertebral or brachial plexus nerve blocks.
- Interpleural, epidural or intrathecal analgesic infusions.
- Local thoracic spine neurolytic blocks.
- Percutaneous cervical cordotomy (particularly when the patient is still ambulant).

In pain from chest wall involvement the response to opioids is variable because of added inflammatory and neuropathic components. In this situation, the following adjuvant analgesics should be considered early: non-steroidal anti-inflammatory drugs (with gastric cover); steroids (with gastric cover); noradrenergic antidepressants such as amitriptyline; or anticonvulsants such as gabapentin or carbamazepine. Pain control will be improved by attention to emotional, psychological, social and spiritual problems. Distraction and relaxation techniques and complementary therapies may also be helpful. Pain associated with localised tumour invasion of the chest wall may respond to radiotherapy.

14. Follow-up

14.1 Post treatment Review

The MDT should note the completion of treatment(s) (chemotherapy, radiotherapy or surgery) and a decision about who should lead follow-up be agreed.

A review of the patient's treatment to date should be made with an indication of the prognosis noted. Persisting clinical problems should be noted along with decisions about their management. Any further clinical developments should be anticipated and advice given about what to do if they materialise should be given.

This should form the basis of a letter to the GP (copy to the patient):

- Diagnosis and staging
- Treatment given and assessment of their likely effect
- Current symptoms and management plan
- Prognosis
- Expected complications and any provisional management plan
- Services and agencies already involved in care
- How to contact other services which may be needed
- Information given to patient and carers

14.2 Follow up appointments

These will depend on the patient's condition and clinical opinion and local arrangements will apply. For patients who have undergone attempted curative surgery follow-up should be for at least 9 months, but no more than 5 years.

15. Clinical Trials

15. Clinical Trials

Where appropriate, patients are best treated in a clinical trial setting. The network strongly supports entry of patients into NCRN trials.

16. Referral to other MDTs

16. Referral to Other MDTs

In certain circumstances, it may be necessary to seek the expertise of another MDT, either within or outside the network. This may be an MDT dealing with the same tumour site, or a different tumour site.

These referrals should be made promptly to the lead clinician of the MDT in question, usually by means of a faxed referral letter containing all the relevant information. It is noted that a telephone call to a member of that MDT may be helpful.

17. Lung Cancer Waiting Times

The NHS Cancer Plan was published in September 2000. Within the Plan there were a number of service standards relating to waiting times for outpatient services and hospital treatment. These Service Standards are:

- 2 week standard from urgent GP referral for suspected cancer to first hospital assessment
- 31 day standard from decision to treat to first treatment
- 62 day standard from urgent GP referral for suspected cancer to first treatment

The Cancer Reform Strategy published in December 2007 noted that these service standards did not apply to all cancer patients or treatments and they were therefore expanded to extend the range of patients who could benefit. These Service Standards were extended:

- The 31 day standard includes subsequent treatments for all cancer patients including those diagnosed with a recurrence
- A consultant upgrade to the 62 day pathway is applied where cancer is suspected; this can apply to cancer screening programmes where suspected cancer is detected (not currently available for lung cancer).

All correspondence or requests for procedures should clearly highlight that the patient is on a cancer pathway and where applicable, target dates should be specified.

18. Useful references

British Thoracic Society Radiologically-Guided Lung Biopsy guidelines: http://www.brit-thoracic.org.uk/ClinicalInformation/RadiologicallyGuidedLungBiopsy/RadiologicallyGuidedLungBiopsyGuideline/tabid/141/Default.aspx

7th UICC Lung Cancer TNM Staging System [Ann Thorac Surg 2009 15:4-9]
British Thoracic Society Bronchoscopy in Adults 2013
https://www.brit-thoracic.org.uk/document-library/clinical-information/bronchoscopy/flexible-bronchoscopy/diagnostic-flexible-bronchoscopy-in-adults-guideline-2013/

British Thoracic Society Advanced Bronchoscopy Guidelines
https://www.brit-thoracic.org.uk/document-library/clinical-information/bronchoscopy/advanced-diagnostic-and-therapeutic-bronchoscopy/bts-advanced-bronchoscopy-guideline/

British Thoracic Society Fitness for Surgery Guidelines:
http://www.brit-thoracic.org.uk/ClinicalInformation/Bronchoscopy/BronchoscopyGuidelines/tabid/120/Default.aspx

NICE lung cancer guidelines (updated May 2011)
http://guidance.nice.org.uk/CG121

Royal College of Pathologists Lung Cancer Data Set 2007
http://www.rcpath.org/Resources/RCPath/Migrated%20Resources/Documents/G/G048_LungDatasetMay14.pdf

Tissue Pathways for Pulmonary Pathology 2008
http://www.rcpath.org/Resources/RCPath/Migrated%20Resources/Documents/G/G135_TPThoracic_Jun13.pdf

Quality Assurance in Histopathology and Cytopathology Reporting Practice 2009
http://www.rcpath.org/

Appendix 1 – TNM Staging Classification of Lung Cancer

The TNM Classification of Malignant Tumours, 7th edition, is used to stage lung cancer.

Radiological staging should be included in the report on a staging CT scan. Final staging (prior to mediastinal sampling) should be a combined decision made at the MDM.

Table 3.1: TNM classification TNM classification	
T	T = Extent of primary tumour Tis – Carcinoma in situ TX – Positive cytology T1a – The tumour is contained within the lung and is smaller than 2cm across T1b – The tumour is contained within the lung and is between 2cm and 3cm across T2a – >3cm but ≤5cm (or tumour with any other T2 descriptors – main bronchus, >2cm from carina, invades visceral pleura, partial atelectasis – but ≤5cm) T2b – >5cm but ≤7cm T3 – >7cm or growth into chest wall, diaphragm, pericardium, mediastinal pleura, main bronchus <2cm from carina, total atelectasis, phrenic nerve, more than 1 nodule in same lobe T4 – Growth into mediastinum, heart, great vessels, carina, oesophagus, vertebrae, trachea; nodules in more than 1 lobe of the same lung
N	N = Condition of regional nodes N0 – No regional lymph node metastasis N1 – Ipsilateral peribronchial, ipsilateral hilar N2 – Ipsilateral mediastinal, subcarinal N3 – Contralateral mediastinal or hilar, scalene or supraclavicular
M	M = Metastases MX – Distant metastases cannot be assessed M0 – No distant metastases M1a – Separated tumour nodule/s in the contralateral lung: tumour with pleural nodules or malignant pleural effusion/pericardial effusion M1b – Distant metastases

Appendix 2 – CT Protocol

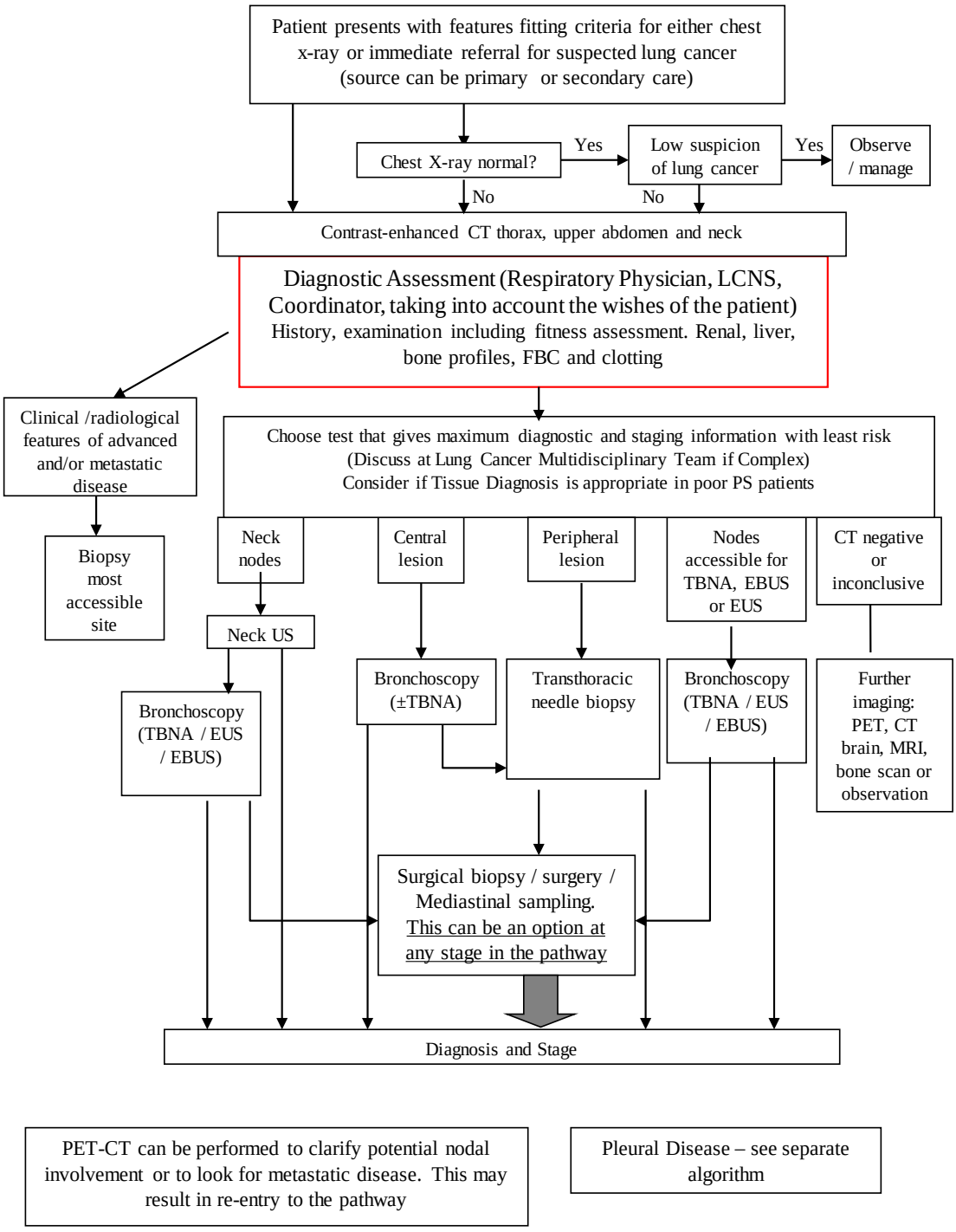
Suggested Standard CT protocol

- 100 mls of 300 mg/dl iodine @ 3 mls/s
- 25 delay for thorax, 60 s delay for upper abdomen (increase if suspected cardiac dysfunction)
- 2 mm collimation or less
- Coverage: Lower neck to lung bases, and top of right hemidiaphragm to inferior aspect of liver
- Scan to pubic ramus if PH of abdominal malignancy or abdominal symptoms or likely metastatic disease
- Include post contrast head if symptoms to suggest cerebral metastases or if difficulty with clinical assessment (e.g mental impairment)

Suggested Pleural CT protocol

- 100 mls of 300 mg/dl iodine @ 3 mls/s
- 60 s delay
- 2 mm collimation or less
- Coverage: Lower neck to inferior aspect of liver. Include pelvis if female patient (Ovarian cancer) or if PH of abdominal malignancy or abdominal symptoms or likely metastatic disease

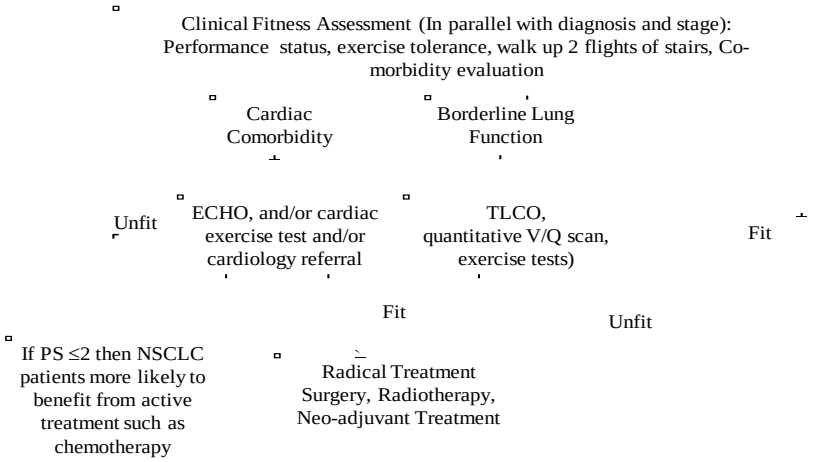
Appendix 3 – Diagnostic and Staging Clinical Pathway



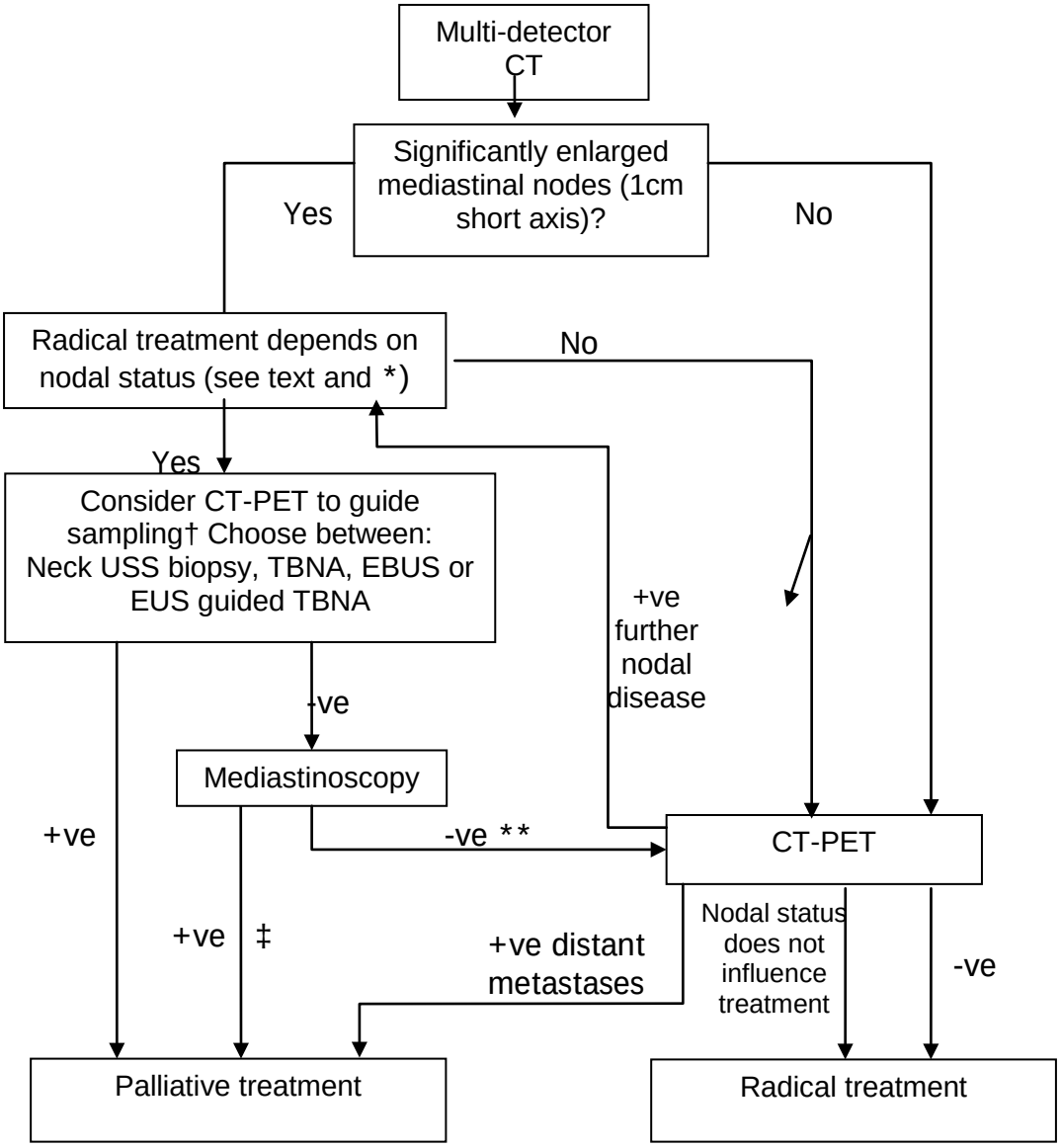
PET-CT can be performed to clarify potential nodal involvement or to look for metastatic disease. This may result in re-entry to the pathway

Pleural Disease – see separate algorithm

Appendix 4 – Fitness Assessment Clinical Pathway for Radical Treatment



Appendix 5 - Investigation Pathway for Mediastinal Diagnosis and Staging

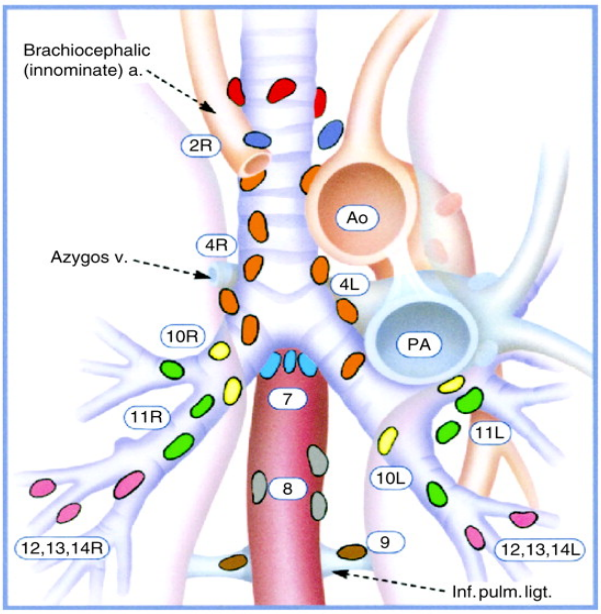


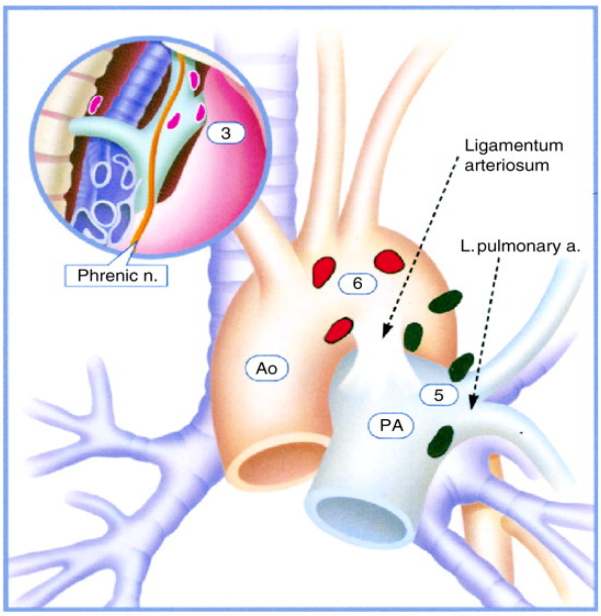
* **For example, if a positive node would preclude or modify radical treatment**

† MDTs may choose to clarify if certain stations are FDG avid prior to sampling

**** Further PET-CT not required if done as part of earlier investigation**
Pathway adopted from BTS guidelines

‡ Except single station N2 disease which may be considered for surgical resection





Superior Mediastinal Nodes

- **1** Highest Mediastinal
- **2** Upper Paratracheal
- **3** Pre-vascular and Retrotracheal
- **4** Lower Paratracheal (including Azygos Nodes)

N_2= single digit, ipsilateral
N_3= single digit, contralateral or supraclavicular

Aortic Nodes

- **5** Subaortic (A-P window)
- **6** Para-aortic (ascending aorta or phrenic)

Inferior Mediastinal Nodes

- **7** Subcarinal
- **8** Paraesophageal (below carina)
- **9** Pulmonary Ligament

N_1 Nodes

- **10** Hilar
- **11** Interlobar
- **12** Lobar
- **13** Segmental
- **14** Subsegmental

Nodal Sampling Techniques

Mediastinoscopy/Mediastinotomy- any mediastinal node
EBUS stations 1,2,3,4,7,10, (11)

EUS stations 2R, 4L, 7, 8, (9)

Appendix 6 – Suspected Pleural Disease Pathways