

FOREWORD

by Finbarr O'Connell

Lung cancer is the leading cause of cancer mortality in Ireland causing approximately 20% of all cancer deaths. Incidence in Irish men has fallen slightly in recent years and is below the EU average, but in Irish women is on the increase and is more than double the EU average. Lung cancer is likely to eclipse breast cancer as the leading cause of cancer mortality in Irish women in the near future and has already done so in some other countries.

Unfortunately, despite the enormous burden of disease, the prevailing attitude to lung cancer, even among health care professionals, is one of pessimism, or at worst, absolute nihilism. This reflects poor overall survival rates, even in the minority of patients who present with apparent early-stage disease who are treated with intention to cure. Overall 5-year survival is less than 10% and despite advances in radiotherapy and chemotherapy, surgery remains the only effective curative treatment for lung cancer. Furthermore, lung cancer is almost entirely preventable as almost 95% is due to cigarette smoking. So why bother with this disease?

First, because the burden of lung cancer is unlikely to diminish significantly, at least in the short term. Smoking prevalence in Irish teenagers is at least as high as that of Irish adults and smoking addiction, once established, is difficult for the individual to beat. Furthermore, almost 50 years after the link between tobacco and lung cancer was first established, the tobacco industry is thriving and seems unlikely ever to plead “guilty as charged”. So the burden of lung cancer remains, and in women is increasing at an alarming rate.

Second, and more important, because there is ample evidence that improved organisation of lung cancer services, with rapid access to multidisciplinary care, improves outcome. As things stand, services for lung cancer are disorganised and fragmented, and the care offered to the individual patient may depend more on geographical location than tissue diagnosis and stage. It is surely an indictment of lung cancer care in Ireland that rates of tissue diagnosis are much lower than for other cancers and accurate staging information is available for only 37% of cases. Furthermore, approximately 50% of patients with lung cancer are offered no treatment other than palliative care. Yet, the evidence is clear that early referral with rapid access to well organised multidisciplinary care leads to improved short and long term survival with better quality of life.

It is against this background that the All-Ireland lung cancer working group first met just over 2 years ago to try to put lung cancer “on the agenda” and begin the process of improving lung cancer care in Ireland. These guidelines represent a consensus view of that group, endorsed by the Irish Thoracic Society, the Irish Society of Medical Oncology, the Irish Clinical Oncology Research Group and many specialists involved in various aspects of lung cancer care in Ireland who attended the second All-Ireland Lung Cancer conference last year.

While recognising the enormous importance of other areas such as prevention and research, the principal focus of these guidelines is on clinical management. It is hoped that this document will assist general practitioners in lowering their threshold for early referral and in gaining rapid access to appropriate local services. It is also hoped that this document will assist those at hospital level to organise well defined care pathways for early diagnosis and staging and rapid referral to appropriate multidisciplinary lung cancer care. Ultimately, such basic steps will improve outcome for lung cancer patients in Ireland.

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INTRODUCTION AND BACKGROUND INFORMATION

- Lung cancer is the leading cause of cancer mortality in Ireland representing approximately 20% of all deaths due to cancer
- 2332 new cases per year - 793 female, 1539 male
- 2301 deaths per year - 790 female, 1511 male
- In women -
 - 4th most common cancer site 2nd most common cause of cancer death
 - 6.5% of new cancer cases 15.4% of cancer deaths
- In men -
 - 3rd most common cancer site Most common cause of cancer death
 - 11.9% of new cancer cases 25.7% of cancer deaths
- The female:male ratio for lung cancer has risen from 1:10 in 1978 to 1:2 in 1996 and continues to rise.
- Compared to other EU countries, incidence rates for men are below average but for women are almost twice the EU average.
- <1% of cases occur before age 40, rates rise steeply after age 40 and peak at 65-70.
- Over 90% of lung cancer may be attributed to smoking tobacco and is therefore theoretically preventable. However, the prevalence of smoking in Irish adults is still 29% and in teenagers is >30%. Smoking is more common among lower socio-economic groups and is increasing in women.
- The success rate for smoking cessation among established smokers is 10% with non-pharmacological means and 20% with additional nicotine replacement therapy. Therefore, lung cancer will continue to be a major cause of cancer mortality for the foreseeable future.
- Currently >75% of patients present with advanced stage disease.
- Earlier diagnosis, efficient and correct diagnosis and staging, and modern multidisciplinary management lead to improved short and long term survival with good quality of life.
- All of the services necessary for excellent lung cancer care currently exist in Ireland. However, improvements in the delivery of this care are necessary through earlier diagnosis, rapid access to diagnostic and staging procedures, and provision of co-ordinated multidisciplinary treatment.

Data from *All-Ireland cancer statistics 1994-96*, a joint report on incidence and mortality for the island of Ireland, NI Cancer Registry and National Cancer Registry Ireland

AIMS OF THE GUIDELINES

- to raise awareness of lung cancer among health care professionals, health care providers, patients and the general public
- to assist in the provision to all patients of rapid access to high quality multidisciplinary lung cancer care

INITIAL PRESENTATION AND ACCESS TO DIAGNOSTIC SERVICES

Rapid access to appropriate multidisciplinary care improves outcome in lung cancer.

In most cases, initial presentation will be to the GP, but in some cases will be to A+E departments or other agencies. CXR will be available at presentation in A+E. For GPs, when there is a genuine clinical suspicion, CXR should be available at their local hospital within 1 week and preferably on a walk-in basis. Indications for urgent chest x-ray in the over 30 age group, particularly smokers/ex-smokers, are shown in Table 1. Where the CXR is suggestive or suspicious of tumour, and/or the clinical suspicion is high, respiratory/medical OPD should be available within 1 week of receipt of request from GP or A+E for assessment.

The overall care pathway of the lung cancer patient is shown in Figure 1. Ideally, diagnosis, staging and multidisciplinary assessment should be completed, and a decision made on appropriate primary therapy, within 4 weeks of initial referral.

Chest Xray

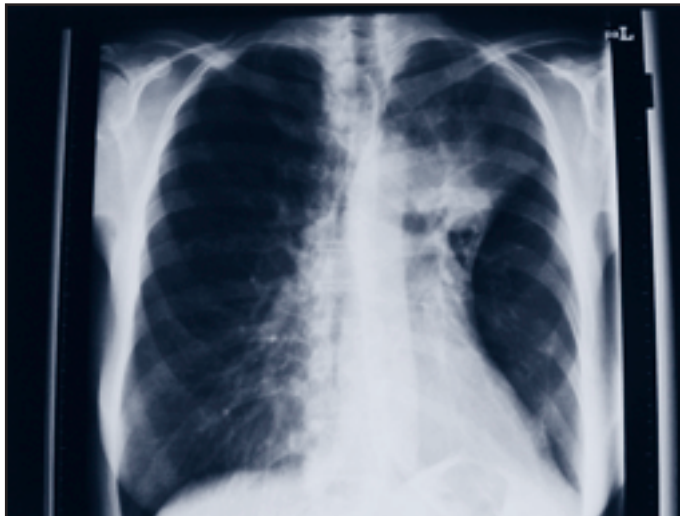


TABLE 1

Indications for Urgent Chest X-ray

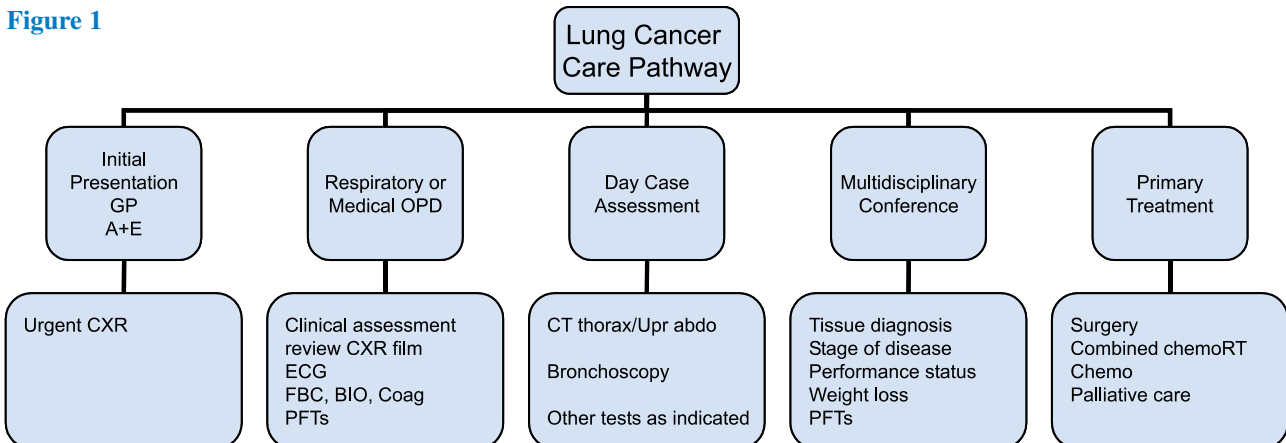
Symptoms –

- Haemoptysis
- New onset unexplained cough or alteration in character/severity of chronic cough
- Unexplained chest pain or dyspnoea
- Unexplained weight loss/cachexia
- Unexplained bone pain/neurological symptoms

Signs –

- Clubbing
- Lymphadenopathy
- Focal chest signs
- Hepatomegaly

Figure 1



ACTIVE MANAGEMENT OF LUNG CANCER

In order to manage lung cancer appropriately, the following information is required –

- 1 Tissue diagnosis
- 2 Clinical stage
- 3 Assessment of general medical condition (performance status), co-morbidity and weight loss
- 4 Pulmonary function, particularly where surgery, radical radiotherapy or chemotherapy under consideration

Tissue diagnosis will usually be obtained at bronchoscopy and may be confirmed by cytology/histology from other sites such as lymph glands, skin nodules or pleural fluid etc. Clinical staging always requires clinical evaluation, biochemistry, bronchoscopy and CT thorax and upper abdomen. Performance status, co-morbidity, weight loss and pulmonary function are easily assessed at initial clinical evaluation. Ideally, these investigations should be organised on 2-3 days as follows

Day 1	Clinical assessment, blood tests and pulmonary function
Day 2/3	CT thorax/upper abdomen and bronchoscopy

It may not always be possible or appropriate to arrange CT on the same day as bronchoscopy. Also, completion of staging may require other investigations depending on symptoms, signs, biochemistry or CT results.

Initial Assessment at Respiratory/Medical OPD

The key components of the initial assessment at respiratory/medical OPD are shown in Table 2.

TABLE 2

Initial Assessment at Respiratory/Medical OPD

Full clinical evaluation including specific assessment of -

- performance status/general medical condition
- co-morbidity
- weight loss
- bone pain
- hoarseness
- superior mediastinal obstruction (superior vena cava syndrome)
- neurological symptoms, brachial neuritis, Horner's syndrome
- lymphadenopathy, especially cervical
- skin nodules
- hepatomegaly
- paraneoplastic syndromes (Table 7)

Review CXR film

ECG

Blood tests

- FBC
- Coagulation screen
- biochemistry (renal, liver and bone)

Pulmonary function tests (if available)

Arrange investigations required for tissue diagnosis and staging –

- bronchoscopy
- CT thorax/upper abdomen (ideally should be carried out prior to bronchoscopy)
- other necessary investigations based on clinical evaluation

PERFORMANCE STATUS, CO-MORBIDITY AND WEIGHT LOSS

General medical condition should be assessed in detail and may be formally assessed according to either the ECOG scoring system (Table 3) or Karnovsky index (Table 4). Weight loss should be estimated at initial assessment and actual weight documented at each clinic visit. As most patients with lung cancer are smokers, smoking-related co-morbidity is prevalent. Other co-morbidity must also be taken into account, particularly in patients under consideration for surgery, chemotherapy or radical radiotherapy. Conditions which tend to dictate against these therapies include –

- cachexia
- severe ischaemic heart disease eg) unstable angina or heart failure poorly responsive to medical therapy
- severe COPD (see pulmonary function below)
- severe smoking-unrelated co-morbidity which carries increased risk for surgery/chemotherapy/radical RT or has profound implications for quality of life, cognitive function etc.

TABLE 3	
<i>ECOG Performance status</i>	
0	No symptoms. <i>Able to carry out all normal activities without restriction</i>
1	Symptoms <i>Restricted in physically strenuous activity but ambulatory and able to carry out light work</i>
2	Ambulatory and capable of all self-care but unable to carry out any work <i>Up and about more than 50% of waking hours</i>
3	Capable of only limited self-care. <i>Confined to bed or chair more than 50% of waking hours</i>
4	Completely disabled and unable to carry on any self-care. <i>Completely confined to bed or chair</i>

TABLE 4	
<i>Karnovsky Index</i>	
Status	Score
Normal, no complaints	100
Able to carry on normal activities	90
Minor symptoms or signs of disease	
Normal activity with effort	80
Cares for self.....	70
Unable to carry on normal activity or do active work	
Requires occasional assistance but able to care for most needs.....	60
Requires considerable assistance and frequent medical care	50
Disabled	40
Requires special care and assistance	
Severely disabled	30
Hospitalization indicated though death not imminent	
Very ill.....	20
Hospitalization and active supportive treatment necessary	
Moribund.....	10
Dead	0

PULMONARY FUNCTION AND ARTERIAL BLOOD GASES

Pulmonary Function

Pulmonary function is essential for patients under consideration for surgery, chemotherapy or radical radiotherapy. For patients undergoing surgery –

- Pre-operative FEV1 > 2l indicates pneumonectomy should be well tolerated.
- If pre-op FEV1 < 2l, predicted post-op FEV1 should be calculated based on the pre-op value and the fractional functional contribution of the lung to be resected. This can be estimated with quantitative perfusion lung scanning or from the following equation -
- Post-op FEV1 = Pre-op FEV1 x [A - (B - C)]/A where
A = no of bronchopulmonary segments present pre-op (19 unless patient had previous surgery)
B = no of bronchopulmonary segments to be resected
C = no of bronchopulmonary segments to be resected which are non-functional
- Predicted post-op FEV1 > 40% normal or > 800 ml favours surgery especially when gas transfer is normal. Surgery will be less well tolerated when gas transfer is impaired.
- For borderline cases who do not fulfil above criteria, cardiopulmonary exercise testing may be considered. VO2 max > 15 ml/kg favours surgery.

Arterial Blood Gases

- Hypoxaemia is not a contraindication to surgery and may improve after surgery where there is poor local ventilation due to collapse/atelectasis.
- Hypercapnia has traditionally been considered to increase risk significantly, and while this has not been proven and some studies suggest otherwise, severe hypercapnia should be considered a significant risk factor.

TISSUE DIAGNOSIS

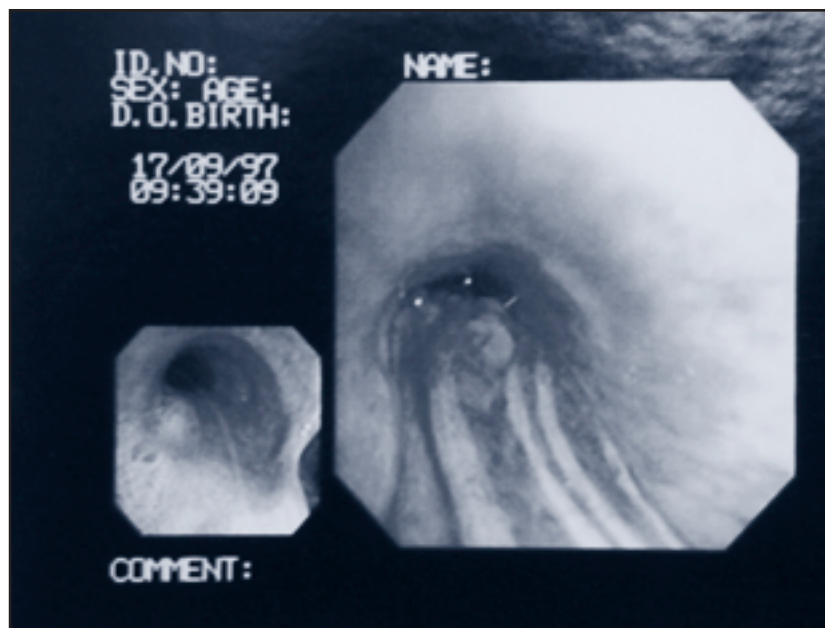
Bronchoscopy will usually provide tissue diagnosis and will also provide information essential for staging. The following diagnostic procedures may be carried out during bronchoscopy-

- Visible lesions - lavage
brushings (particularly diffuse lesions)
endobronchial biopsies
- Peripheral lesions - lavage
± transbronchial biopsies
± transbronchial needle aspirate
- Central lesions not visible transbronchial/transtracheal needle

Mediastinal lymph node sampling may also be carried out during bronchoscopy (see below under staging) and may provide the tissue diagnosis where the primary lesion is not visible within the airway. Where bronchoscopy is non-diagnostic, tissue diagnosis may be obtained by other procedures some of which may be required for staging in any case -

- Fine needle aspirate (FNA) of palpable lymph glands
- FNA of skin nodules
- Pleural aspirate (± biopsy)
- Percutaneous FNA (or Tru-cut biopsy) of –
 - primary lung lesion
 - satellite lung lesions
 - mediastinal lymph nodes
- Mediastinoscopy, Mediastinotomy, Thoracotomy

Bronchoscopy



STAGING

Non-small cell lung cancer is staged according to the TNM Classification system (Table 5). Significant changes in the staging of NSCLC were introduced in 1997 as follows -

- satellite nodules within same lobe as primary = T4
- satellite nodules in ipsilateral non-primary lobe = M1
- subdivision of stages I and II into a and b
- reclassification of T3N0M0 from IIIa to IIb

Small cell lung cancer is staged as limited or extensive stage (Table 6).

TABLE 5

Staging of Non-Small Cell Lung Cancer (TNM classification)

Primary Tumour T

T0	no evidence of primary
Tis	CIS
T1	3cm or less in max diameter, no invasion of visceral pleura, no invasion proximal to a lobar bronchus
T2	>3cm max diameter, involvement of mainstem bronchus >2cm from main carina invasion of visceral pleura atelectasis/obstructive pneumonitis extending to hilum but not entire lung
T3	invasion of chest wall, diaphragm, mediastinal pleura, parietal pericardium mainstem bronchus <2cm from main carina, but not involving main carina atelectasis/obstructive pneumonitis of entire lung
T4	mediastinum, heart, great vessels, trachea, oesophagus, vertebra, main carina malignant pleural or pericardial effusion satellite nodules within same lobe as primary tumour

Lymph Nodes N

N0	no nodal involvement
N1	ipsilateral peribronchial, intrapulmonary and/or hilar nodes by direct invasion or metastasis
N2	ipsilateral mediastinal and/or subcarinal nodes
N3	contralateral hilar or mediastinal nodes ipsilateral or contralateral scalene or supraclavicular nodes

Distant Metastasis M

M0	no distant metastasis
M1	distant metastasis or satellite pulmonary nodules in separate lobe from primary

Overall Stage

0	Tis	N0	M0
Ia	T1	N0	M0
Ib	T2	N0	M0
IIa	T1	N1	M0
IIb	T2	N1	M0
	T3	N0	M0
IIIa	T3	N1	M0
	T1-3	N2	M0
IIIb	T any	N3	M0
	T4	N any	M0
IV	T any	N any	M1

TABLE 6

Staging of Small Cell Lung Cancer

Limited Stage - confined to a single radiotherapy port

- one hemithorax
- mediastinum
- ipsilateral supraclavicular nodes
- no pleural effusion
- (equivalent to Stages Ia to IIIa/b NSCLC)

Extensive Stage –

- disease beyond limited stage
- (equivalent to Stage IIIb/IV NSCLC)

TABLE 7

Paraneoplastic syndromes which may be associated with lung cancer

Malaise, anorexia, weight loss, cachexia

Anaemia

Digital clubbing

Hypertrophic pulmonary osteoarthropathy (HPOA)

Endocrine syndromes –

- syndrome of inappropriate antidiuresis (SIADH)
- Cushing’s syndrome (ACTH)
- Hypercalcaemia (PTH) – may also be due to bony metastases

Neuromyopathies –

- peripheral neuropathy
- cerebellar syndrome
- encephalopathy
- proximal myopathy
- polymyositis
- dermatomyositis
- Eaton-Lambert syndrome

Vascular –

- Thrombophlebitis migrans
- non-bacterial endocarditis

STAGING PROCEDURES

Clinical assessment and serum biochemistry will have been carried out at initial assessment. Bronchoscopy and CT thorax/upper abdomen are essential for staging in all patients. Other staging investigations are not routinely required for most patients but may be required in individual patients depending on results of clinical evaluation, biochemistry, bronchoscopy and CT.

Clinical assessment (all patients)

Specific features on clinical evaluation may assist accurate staging –

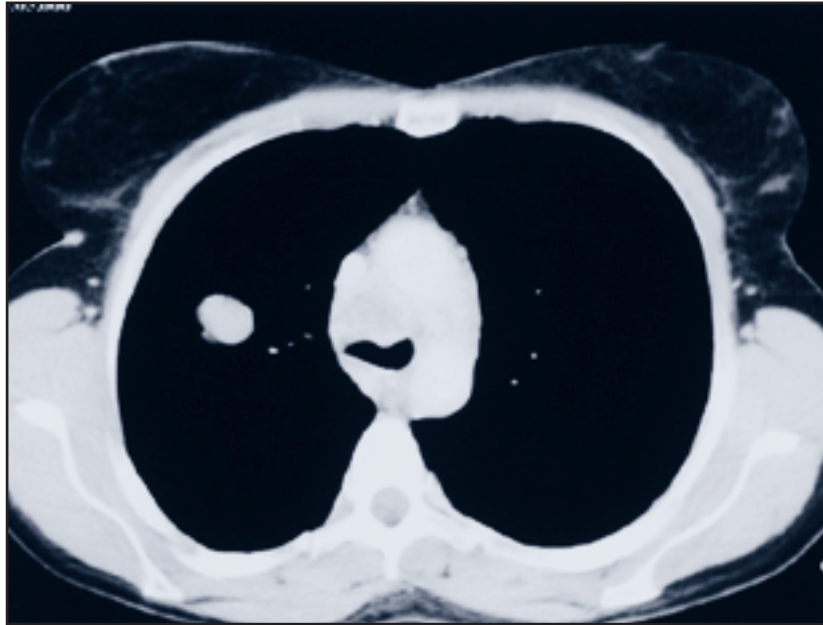
- hoarseness may indicate recurrent laryngeal nerve palsy
- Horner’s syndrome usually indicates nerve involvement
- superior mediastinal obstruction (SVC syndrome) indicates N2/3 and/or T4 disease
- lymphadenopathy usually indicates N3 disease (easily sampled by FNA)
- skin nodules may be metastatic M1 disease (easily sampled by FNA)
- hepatomegaly (will be evaluated by CT)
- bone pain (will require isotope bone scan / plain films / PET scan)
- neurological symptoms (require further evaluation)
- paraneoplastic syndromes (Table 7) do NOT imply metastasis or inoperability

Bronchoscopy (all patients)

In addition to tissue diagnosis, bronchoscopy will provide staging information –

- differentiate T4/T3/T2 in the airway, i.e. main carina/main bronchus/more peripheral
- rule out second airway lesion(s) undetected by CXR/CT
- sampling of N2 glands helpful when positive BUT insensitive – unhelpful when negative

CT Thorax



CT thorax and upper abdomen (all patients)

All patients should have CT of thorax and upper abdomen as far as the adrenal glands. This provides the most important clinical staging information and the report should include detailed description of the primary lesion, satellite lesions if present, nodal involvement and metastases (Table 8).

TABLE 8

Template for reporting of CT Thorax and Upper Abdomen in Lung Cancer Patients

Primary Lesion

- dimensions
- location - lung(s), lobe(s), segment(s)
- involvement of visceral pleura and fissures
- invasion of mediastinum, chest wall, diaphragm
- for main stem lesions, proximity to, or involvement of, main carina
- atelectasis

Satellite Lesions

- within same lobe
- within same lung
- contralateral lung

Nodal Involvement

- report ATS nodal stations (see map – Figure 2)
- size of involved nodes (<1cm usually reactive, >2cm usually pathologically involved)

Metastases

- liver
- adrenals
- contralateral lung
- bones, skin etc

Figure 2: AJC Classification of Regional Lymph Nodes

Mediastinal (N2) Nodes

Superior mediastinal nodes

- 1 Highest mediastinal
- 2 Upper paratracheal
- 3 Pre and retrotracheal
- 4 Lower paratracheal (incl azygos)

Aortic nodes

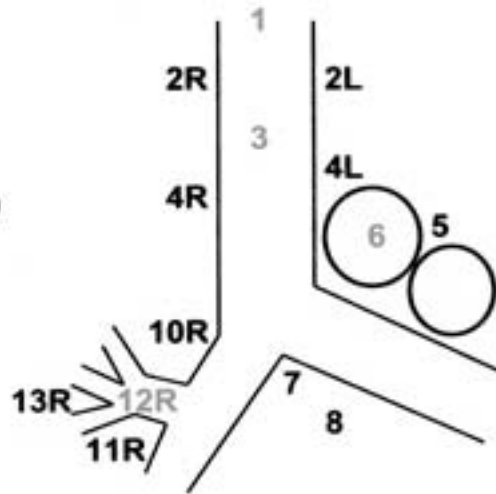
- 5 Subaortic (aortopulmonary window)
- 6 Para-aortic (ascending aortic)

Inferior mediastinal nodes

- 7 Subcarinal
- 8 Paraesophageal (below carina)
- 9 Pulmonary ligament

Bronchopulmonary (N1) Nodes

- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental



Mediastinal lymph node sampling

Where surgery is a consideration, but CT shows mediastinal lymph node enlargement, sampling is required to differentiate malignant from benign reactive nodes –

- Mediastinoscopy allows access to the upper mediastinal (1, 2R, 2L, 3) and right lower paratracheal (4R) lymph node stations.
- Left anterior mediastinotomy may allow access to the left paratracheal (4L), aortopulmonary window (5), supra-aortic (6) and subcarinal (7) stations.
- Transbronchial needle aspiration of paratracheal and subcarinal nodes may be attempted at initial diagnostic bronchoscopy. When positive, this will preclude the need for mediastinoscopy, but the technique is insensitive and negative results are unreliable.
- Endobronchial ultrasound is a relatively new technique which may improve localisation and sampling of paratracheal and subcarinal nodes. Similarly, transoesophageal ultrasound may facilitate sampling of posterior mediastinal, subcarinal and aortopulmonary window nodes.

Pleural aspiration cytology

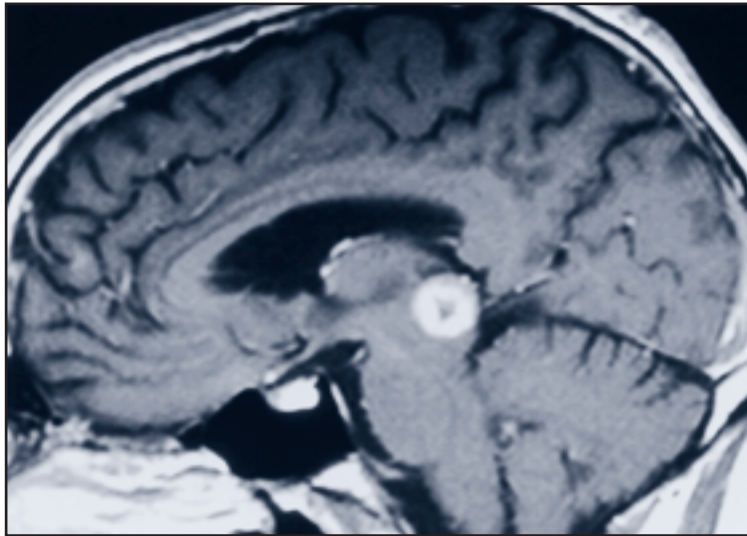
- Where pleural effusion is present, aspiration is essential to try differentiate malignant from benign reactive effusion. When the effusion is clinically apparent, this may easily be carried out at the same time as diagnostic bronchoscopy. Closed pleural biopsy may also be carried out. For smaller effusions, localisation may be improved by radiological guidance with ultrasound or CT.

CT brain (selected patients)

CT detects brain metastases in 3% of asymptomatic patients and therefore should not be carried out routinely BUT should be carried out –

- if headache or other unexplained neurological symptoms/signs are present
- for adenocarcinoma of higher stage than T1N1 where surgery is under consideration

MRI Brain



MRI brain (selected patients)

MRI is more sensitive than CT for early metastases and should be carried out –

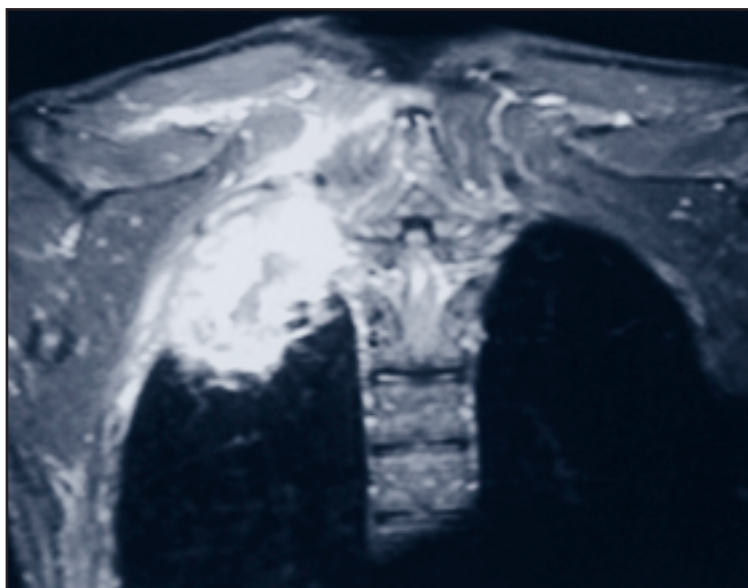
- when CT brain is negative but symptoms/signs suggest possible cerebral metastases

MRI thorax (selected patients)

MRI is better than CT for detection of direct invasion and should be carried out in selected patients –

- where surgery is under consideration and CT suggests possible direct invasion by primary tumour of adjacent structures such as –
 - chest wall
 - diaphragm
 - root of the neck
 - mediastinal structures

MRI Thorax



MRI upper abdomen (selected patients)

MRI is superior to CT in differentiating small adrenal metastases from benign adrenal adenomas and should be carried out –

- where CT demonstrates adrenal enlargement which is not obviously metastatic

Ultrasound of Abdomen (selected patients)

U/S should be carried out -

- where CT shows single hepatic or renal lesions which are probably benign and better characterised by ultrasound

Isotope bone scan (selected patients)

Isotope bone scan is almost always negative when there is no bone pain and the bone chemistry is normal. It should be carried out –

- if bone pain is present
- if bone chemistry is abnormal

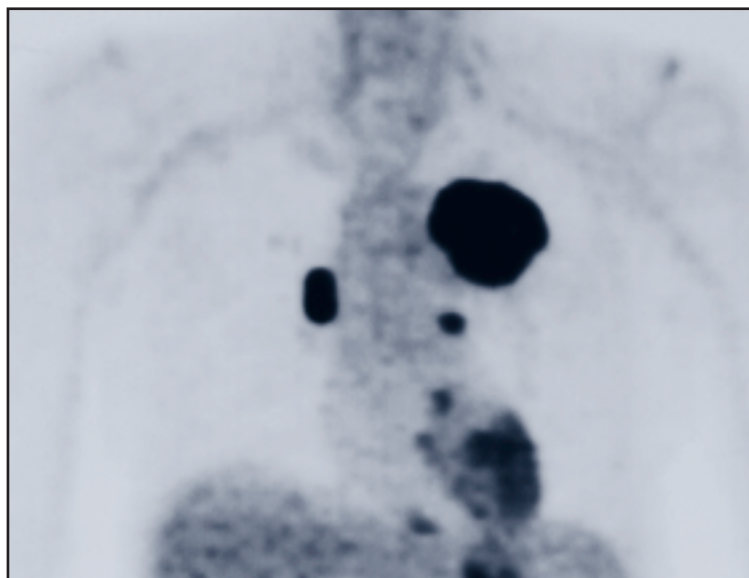
Positron Emission Tomography (PET) (selected patients)

Lung cancer cells typically have a high avidity for fluoro-deoxy-glucose (FDG) used for PET scanning. Early data in lung cancer are very promising and PET is likely to play an increasing role particularly where surgery or radical RT is under consideration and –

- second intra-pulmonary nodules are present
- mediastinal glands are present, not easily accessible by mediastinoscopy/mediastinotomy
- other inaccessible lesions are present

In due course, multi-modality CT/PET scanning is likely to play an increasing role in the pre-operative work-up of patients being assessed for curative surgery or radical RT.

PET Scan



PRIMARY TREATMENT

Appropriate management of lung cancer requires the following information –

- 1 **Tissue diagnosis**
- 2 **Clinical stage**
- 3 **Assessment of general medical condition (performance status), co-morbidity and weight loss**
- 4 **Pulmonary function, particularly where surgery, radical radiotherapy or chemotherapy under consideration**

Ideally, as soon as this information is available, all patients should be discussed at a multidisciplinary forum with access to a full lung cancer team so that appropriate primary treatment and follow-up can be arranged efficiently and effectively (Table 9). Where access to a multidisciplinary forum is not easily available, consultation with or advice from an appropriate specialist with an interest in lung cancer should be arranged. Depending on the likely primary treatment and local availability of various specialties, appropriate initial consultation may include –

- respiratory medicine
- thoracic surgery
- medical oncology
- radiation oncology

TABLE 9

The Multidisciplinary Lung Cancer Team

Appropriate team members –

- nurse coordinator/specialist
- respiratory physician
- radiologist
- cytohistopathologist
- thoracic surgeon
- radiation oncologist
- medical oncologist
- palliative care physician

The extended team should also include or have close working links with –

- nutritionist/dietitian
- pharmacist
- psychologist/psychiatrist
- medical social worker
- pastoral care
- full palliative care team
- general practitioner/primary care team

Treatment of Non-Small Cell Carcinoma

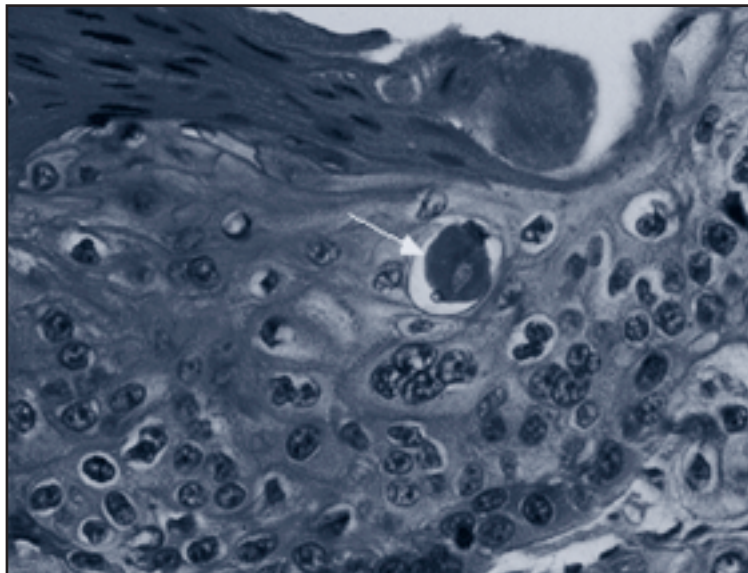
Appropriate primary treatment for NSCLC is determined predominantly by stage of disease, but also by performance status, co-morbidity and weight loss (Table 10). Where performance status is good with minimal co-morbidity and weight loss, surgery, with intention to cure, is appropriate for stage I, II and some IIIA patients. Radical RT or combined chemo/RT should be considered for locally advanced inoperable stage IIIA or IIIB disease. Palliative chemotherapy should be considered for metastatic stage IV disease. These “aggressive” therapies may not be possible where performance status is poor, pulmonary function is inadequate, or there is severe co-morbidity or weight loss. Treatment will then largely be palliative with palliative RT where indicated for symptoms. Obviously each patient must be considered individually.

For a small number of patients with stage I disease, where surgery is not advisable because of medical co-morbidity or inadequate pulmonary function (“medically inoperable disease”), radical RT may be considered, with intention to cure.

TABLE 10
Approach to Treatment of NSCLC

Stage	Performance status Co-morbidity Weight loss Pulmonary function	good min-mild min-mild adequate	poor severe severe inadequate
I		Surgery	Palliative care Palliative RT where indicated
II		Surgery	Palliative care Palliative RT where indicated
III		± Surgery (T3N1) Radical RT ± Chemo	Palliative care Palliative RT where indicated
IV		± Chemo	Palliative care Palliative RT where indicated

Non-Small Cell Carcinoma (Squamous)



NSCLC with good performance status, minimal co-morbidity and adequate pulmonary function -

Stage IA (T1N0), IB (T2N0), IIA (T1N1), IIB (T2N1)

Surgical resection –

- should include adequate mediastinal lymph node dissection (depending on site/stage)
- should aim to conserve lung where possible through bronchoplastic procedures (sleeve lobectomy rather than pneumonectomy)
- wedge resection or anatomical segmentectomy may be necessary where lobectomy is inadvisable because of inadequate pulmonary function or general medical condition

- close margins and residual disease should be marked at surgery
- surgical specimens should be reported on according to a standard template (Table 11)
- Findings at surgery and on pathology of the resected specimen will determine further action, both at the time of surgery and post-operatively. Where there are positive surgical margins or adverse pathological features (Table 12), adjuvant chemotherapy or radiotherapy may be appropriate for selected patients.

TABLE 11

Template for Histopathology of Surgical Resection Specimens

The histologic tumour type is:

The grade of the tumour is:

The maximum dimension of the tumour is:

SURGICAL RESECTIONS MARGINS:

Bronchial: is involved / uninvolved by tumour

Vascular: is involved / uninvolved by tumour

Hilar soft tissue: is involved / uninvolved by tumour

Invasion into, but not through the visceral pleura by tumour is: present / absent

Invasion through the visceral pleura by tumour is: present / absent

Vascular invasion by tumour is: present / absent

The non-neoplastic lung tissue shows:

STAGING:

“T” DATA: The primary tumour is classified as:

“N” DATA does / does not include data from previous node sampling procedures
(specimen no.)

The regional lymph nodes are classified as:

The total number of lymph nodes examined is:

The total number of lymph nodes involved by tumour is:

Extranodal extension by tumour is: present / absent / not applicable

Separately submitted Station _____ lymph nodes are involved by tumour

Separately submitted Station _____ lymph nodes are uninvolved by tumour

NOTE:

N1 = Stations 10 -13 = Ipsilateral peribronchial or hilar nodes

N2 = Stations 1 - 9 = Ipsilateral mediastinal and / or subcarinal lymph nodes

N3 = Metastases to contralateral mediastinal / hilar nodes or metastases to ipsilateral / contralateral scalene or supraclavicular lymph nodes

“M” DATA: The status of distant metastasis (includes separate tumour nodules in a different lobe) is:

The overall AJCC STAGE is:

ADDITIONAL COMMENTS:

TABLE 12

NSCLC – Adverse Pathological Features

- inadequate mediastinal lymph node dissection
- multiple positive hilar nodes or any positive mediastinal nodes
- close or positive margins
- extracapsular spread
- lymphovascular or perineural invasion
- high histological grade/poor differentiation

Stage IIB (T3N0) and IIIA (T3N1)

Superior sulcus	resectable	RT±chemo then surgery or surgery then RT±chemo
	unresectable	RT±chemo then re-evaluate for resectability
Chest wall or Proximal airway or Mediastinum	resectable	Margins negative - Observe
	unresectable	Margins positive - Re-resect or RT±chemo RT±chemo then re-evaluate for resectability

Stage IIIA (T1-3N2)

Radical RT or Consider chemo/RT -		
• chemotherapy x 2 courses	progression	RT
	regression or stable	complete chemo x 4-6 plus RT

Stage IIIB (T1-3N3)

Consider chemo/RT as for IIIA

Stage IIIB (T4N0-1)

Resectable satellite lesion	surgery	consider adjunctive chemo
Resectable local invasion	surgery	consider adjunctive chemo
Unresectable	RT or chemo/RT as for IIIA	

Stage IIIB (T4N2-3)

Consider chemo/RT as for IIIA

Stage IIIB (T4 pleural effusion)

Local therapy if necessary - pleural drainage ± pleurodesis
Treat as for stage IV disseminated disease

Stage IV (M1 solitary site)

Consider palliative chemoTx as for Stage IV M1 disseminated (see below), or
Best supportive care or

If primary tumour operable by TN stage consider resection after definitive treatment of metastasis -

- adrenal resect
- contralateral lung resect
- brain resect or stereotactic radiosurgery

Stage IV (M1 disseminated)

Best supportive care or

Consider palliative chemo x 2 courses-

- response or stable disease and well tolerated - continue x 4-6 or till progression
- no response or poorly tolerated - best supportive care or consider alternative regime

Chemotherapy in NSCLC

- where possible administer as part of clinical trials
- consider for good performance patients with minimal co-morbidity and inoperable disease
- initial 2 courses and assess response
- if regression (or no progression) consider surgery or radical RT if re-staging suggests all disease can be ablated. Otherwise, continue x 4-6 courses or until progression as tolerated
- combine with RT for locally advanced inoperable stage IIIA (and some IIIB)
- consider in stage IV disease, particularly if no more than 1 extranodal metastatic site
- While surgery at present offers the best chance of cure in NSCLC, 5 year survival rates are nevertheless disappointing, particularly for Stage Ib and II disease. Much attention is currently focussed on the role of neo-adjuvant chemotherapy prior to surgery and recommendations for this approach are likely to evolve over the coming 2-3 years.

NSCLC with poor performance status, significant co-morbidity or inadequate pulmonary function -

Stage I-II Medically Inoperable

Consider radical RT or

Best supportive care with palliative RT where indicated

Stage III-IV

Best supportive care with palliative RT where indicated

Post-operative surveillance

every 3 months year 1 then

every 6 months year 2-3 then

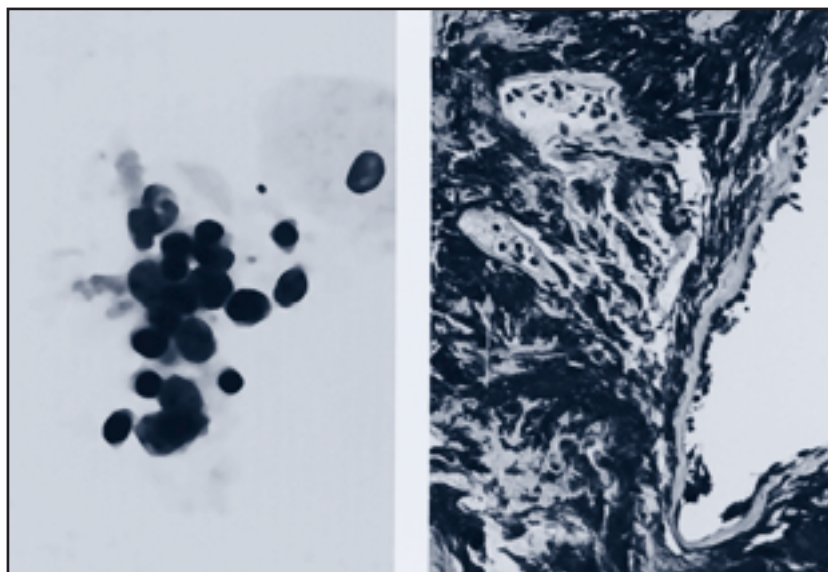
annually

- clinical evaluation
- FBC, biochemistry
- CXR

TABLE 13
Approach to Treatment of SCLC

Stage	Performance status Co-morbidity Weight loss	mod-good min-mild min-mild	poor severe severe
Limited		Chemo + RT PCI	Palliative care Palliative RT where indicated
Extensive		Chemo	Palliative care Palliative RT where indicated

Small Cell Carcinoma



Treatment of Small Cell Carcinoma

Appropriate primary treatment for SCLC is determined predominantly by stage of disease, but also by performance status, co-morbidity and weight loss (Table 13). Where performance status is good with minimal co-morbidity and weight loss, combined chemo/RT should be considered for patients with limited stage disease. RT should be administered early in the chemotherapy schedule. Prophylactic cranial irradiation (PCI) is also indicated in limited stage disease and will usually be administered at the same time as thoracic RT. Where performance status is poor or co-morbidity severe, treatment may largely be palliative. Obviously each patient must be considered individually.

SCLC with moderate-good performance status and mild-moderate co-morbidity -

Limited stage

Chemo and concurrent thoracic RT (which is best given early in the chemo schedule; therefore arrange RT consultation early)

If apparent complete remission, arrange CT brain and prophylactic cranial irradiation (PCI). PCI may already have been administered with thoracic RT.

Extensive stage

Chemotherapy

Cranial RT should be arranged for radiologically-proven cranial metastases

Further management of SCLC based on outcome of primary treatment -

Complete remission lasting 3 months

- Long-term OPD follow up.
- Consider further chemotherapy for relapse

Incomplete remission or apparent complete remission lasting < 3 months

- Good performance status consider alternative regime
- Poor performance status palliative care

Surveillance of SCLC

every 2 months for year 1 then

every 3 months for year 2 then

every 6 months

- clinical evaluation
- FBC, biochemistry
- CXR
- other imaging to assess sites of previous involvement as indicated

PALLIATIVE THERAPIES

Where disease is considered incurable or primary treatment is unsuccessful, the following palliative therapies may be indicated -

Palliative RT

Indications include -

- Bone pain
- Cranial metastases
- Spinal disease
- Major pulmonary collapse/atelectasis
- Haemoptysis
- Superior mediastinal obstruction (superior vena cava syndrome)

Endobronchial therapy including laser, brachytherapy and stenting.

These treatments are principally indicated for stridor or for major pulmonary collapse/atelectasis with symptoms -

- where maximal external beam radiotherapy has been administered and has been unsuccessful, only partially successful or where successful effect is short-lived.
- where short-segment obstruction causing major collapse is easily amenable to treatment.

Oesophageal Stenting for dysphagia due to oesophageal compression or invasion by nodal disease or direct involvement.

Teflon or Surgical medialisation of the left vocal cord for recurrent laryngeal nerve palsy where there is severe hoarseness or recurrent aspiration.

Pleurodesis for symptomatic pleural effusion

Palliative care will ultimately become the principal focus of care for most patients with lung cancer. Consultation with palliative care services should be arranged in timely fashion and transfer to palliative care should occur as seamlessly as possible.

HEALTH PROMOTION AND LUNG CANCER PREVENTION

More than 90% of lung cancer may be attributed to cigarette smoking. Any strategy for lung cancer must therefore be a smoking prevention, smoking cessation, no smoking and anti smoking strategy -

- the policies in relation to smoking must be implemented in full and maintained in all hospitals.
- all smoking patients, with smoking related and unrelated illnesses, must be encouraged to stop smoking at every opportunity, by all staff involved in their care. This should be done in a supportive fashion.
- smoking cessation support groups should be available in all hospitals. These may be run jointly between the respiratory and cardiology nurse specialists and as an integral part of a pulmonary or cardiopulmonary rehab programme.
- Pharmacotherapy/nicotine replacement should be available as needed/indicated.

BIBLIOGRAPHY

All-Ireland cancer statistics – a joint report on incidence and mortality for the island of Ireland 1994-96.
Northern-Ireland cancer registry and National cancer registry Ireland 2001.

Cancer in Ireland 1997 – incidence and mortality
National cancer registry Ireland.

Cancer in Ireland 1994-2002 – incidence, mortality, treatment and survival.
National cancer registry Ireland.

BTS recommendations to respiratory physicians for organising the care of patients with lung cancer.
The lung cancer working party of the British thoracic society standards of care committee.
Thorax 1998, 53, supplement 1.

BTS guidelines on diagnostic flexible bronchoscopy.
Thorax 2001, 56, supplement 1.

Guidance on commissioning cancer services. Improving outcomes in lung cancer.
NHS executive 1998.

The challenge of improving the delivery of lung cancer care.
Muers MF, Holmes WF, Littlewood C.
Thorax 1999, 54, 540-3.

The effective management of lung cancer.
Muers MF, Macbeth F, Wells FC, Miles A.
Aesculapius Medical Press. UK key advances in clinical practice series 2001.

Management of lung cancer.
Scottish intercollegiate guidelines network 1998.
<http://pc47.cee.hw.ac.uk/sign/home.htm>

Smoking cessation guidelines and their cost effectiveness – a guide to effective smoking cessation interventions for the health care system.
Raw M, McNeill A, West R.
Thorax 1998, 53, supplement 5.

LIST OF ABBREVIATIONS USED

ACTH	Adrenocorticotrophic hormone
A+E	Accident and emergency
ATS	American thoracic society
Chemo	Chemotherapy
CIS	Carcinoma in situ
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
CXR	Chest x-ray
ECOG	Eastern cooperative oncology group
EU	European union
FBC	Full blood count
FEV1	Forced expiratory volume in one second
FNA	Fine needle aspirate
GP	General practitioner
HPOA	Hypertrophic pulmonary osteoarthropathy
LDH	Lactate dehydrogenase
NSCLC	Non-small cell lung cancer
OPD	Out-patients department
PCI	Prophylactic cranial irradiation
PET	Positron emission tomography
PTH	Parathyroid hormone
RT	Radiotherapy
SCLC	Small cell lung cancer
SIADH	Syndrome of inappropriate antidiuretic hormone
SVC	Superior vena cava
TNM	Tumour node metastasis
US	Ultrasound