Lung Cancer Clinical Guidelines

Lung NSSG on behalf of NECN

Document Information

<table>
<thead>
<tr>
<th>Title:</th>
<th>NECN Lung Cancer Clinical Guidelines</th>
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<tbody>
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<td>See page 2</td>
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Document Control

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</tbody>
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Lung NSSG members agreed the Guidelines on:

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CONTENTS

List of Contributors ................................................................. 8
North of England Cancer Network.................................................. 9
Terms of Reference ....................................................................... 10
Introduction ................................................................................ 11
  Incidence .................................................................................. 11
  Mortality ................................................................................... 12
  Survival .................................................................................... 12
  Risk Factors ............................................................................. 13
Screening .................................................................................... 14
Public Health and Prevention ......................................................... 15
Referral Guidelines for Suspected Lung Cancer ............................... 16
  General Principles .................................................................... 16
  NECN Referral Pathways ......................................................... 17
  Pathway for patients with suspected lung cancer ....................... 18
  Patient Centred Care ............................................................... 19
  Making a diagnosis ................................................................... 19
  Investigations ........................................................................... 19
  The need for support and information ....................................... 19
  Continuing education .............................................................. 20
Referrals ....................................................................................... 21
  Specific Guidelines for Urgent Referral for Suspected Lung Cancer 21
    General .................................................................................. 21
    Specific – Referral for Chest X-ray ......................................... 22
    Specific - Referral to a Lung Cancer Unit ................................. 23
NSSG GUIDELINES FOR TEENAGE AND YOUNG ADULTS .......... 24
  Appendix 1 – Teenage and Young Adult Pathway for initial Management . 25
  Appendix 2 – Contact Details .................................................... 26
  Appendix 3 – NHS Specialised Services Pathway ....................... 27
Hospital Investigations .................................................................. 29
  General Principles .................................................................... 29
  Specific Considerations .......................................................... 30
Staging .................................................................................................................. 34
Non Small Cell Lung Cancer .................................................................................. 34
Small Cell Lung Cancer .......................................................................................... 36

Multidisciplinary teams .......................................................................................... 38

Communicating the diagnosis ................................................................................. 41
General Considerations ............................................................................................ 41
Framework of Discussion with Patients ................................................................. 44
When to provide information .................................................................................. 47
Discussion about treatment options ....................................................................... 47
Prognosis .................................................................................................................. 48
Documentation ........................................................................................................ 49
Survival Figures ....................................................................................................... 49
Small cell lung cancer .............................................................................................. 49
Non small cell lung cancer ...................................................................................... 50

Informing the Primary Care Team ......................................................................... 51

Specialist Nursing .................................................................................................... 52

Clinical Trials .......................................................................................................... 55

Audit ........................................................................................................................... 57
LUCADA data collection .......................................................................................... 57
Record Keeping .......................................................................................................... 57

National Cancer Waiting Times Targets & Data Collection .................................... 58

Treatment General Principles .................................................................................. 60

Surgery ...................................................................................................................... 62

Non Surgical Management of Lung Cancer ........................................................... 66

Radiotherapy ............................................................................................................ 66
Non-Small Cell Lung Cancer (NSCLC) .................................................................. 66
Radical Radiotherapy ................................................................................................. 66
Continuous Hyperfractionated Accelerated Radiotherapy (CHART) ................. 67
Conventional Radical Radiotherapy ....................................................................... 67
Stereotactic Body Radiotherapy (SBRT) ................................................................. 67
Post-Operative Radiotherapy .................................................................................. 67
Palliative Radiotherapy ............................................................................................. 68
<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Cell Lung Cancer (SCLC)</td>
<td>69</td>
</tr>
<tr>
<td>Thoracic irradiation (TI) in SCLC</td>
<td>69</td>
</tr>
<tr>
<td>Prophylactic Cranial Irradiation (PCI) in SCLC</td>
<td>70</td>
</tr>
<tr>
<td>Trials</td>
<td>71</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>72</td>
</tr>
<tr>
<td>General Principles</td>
<td>72</td>
</tr>
<tr>
<td>Small Cell Lung Cancer (SCLC)</td>
<td>73</td>
</tr>
<tr>
<td>Staging</td>
<td>73</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>73</td>
</tr>
<tr>
<td>Good Prognosis Patients</td>
<td>73</td>
</tr>
<tr>
<td>Poor Prognosis Patients</td>
<td>74</td>
</tr>
<tr>
<td>Clinical trials</td>
<td>75</td>
</tr>
<tr>
<td>Disease Relapse</td>
<td>75</td>
</tr>
<tr>
<td>Non-Small Cell Carcinoma</td>
<td>76</td>
</tr>
<tr>
<td>Neoadjuvant Chemotherapy</td>
<td>76</td>
</tr>
<tr>
<td>Adjuvant Chemotherapy</td>
<td>76</td>
</tr>
<tr>
<td>Combined Chemoradiation</td>
<td>76</td>
</tr>
<tr>
<td>Palliative chemotherapy</td>
<td>77</td>
</tr>
<tr>
<td>Managing Endobronchial Obstruction</td>
<td>78</td>
</tr>
<tr>
<td>Malignant Mesothelioma</td>
<td>80</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>80</td>
</tr>
<tr>
<td>Clinical Features</td>
<td>81</td>
</tr>
<tr>
<td>Prognosis</td>
<td>81</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>82</td>
</tr>
<tr>
<td>Diagnostic Imaging</td>
<td>83</td>
</tr>
<tr>
<td>Pathology</td>
<td>84</td>
</tr>
<tr>
<td>General Management</td>
<td>85</td>
</tr>
<tr>
<td>Treatment Strategy</td>
<td>85</td>
</tr>
<tr>
<td>Surgery</td>
<td>86</td>
</tr>
<tr>
<td>Management of Pleural Effusion</td>
<td>86</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>87</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>87</td>
</tr>
<tr>
<td>Supportive and Palliative Care</td>
<td>88</td>
</tr>
<tr>
<td>Peritoneal Mesothelioma</td>
<td>89</td>
</tr>
<tr>
<td>Benefits and Compensation for Mesothelioma</td>
<td>89</td>
</tr>
<tr>
<td>Mesothelioma References</td>
<td>90</td>
</tr>
<tr>
<td>Thymic Tumours</td>
<td>91</td>
</tr>
<tr>
<td>Introduction</td>
<td>91</td>
</tr>
<tr>
<td>Histological Classification</td>
<td>92</td>
</tr>
</tbody>
</table>
General Guideline References ............................................................... 127

Appendix 1 - Summary of Lung Cancer Imaging - as submitted to the Radiology group ................................................................. 129

Appendix 2 – NECN CHEMOTHERAPY ALGORITHM ...................... 134

Document Control .............................................................................. 134

Chemotherapy General Principles ................................................. 136
  Chemotherapy .................................................................................. 137
  Good Prognosis Patients ................................................................. 137
  Poor Prognosis Patients ................................................................. 138
  Clinical trials .................................................................................. 138
  Disease Relapse .............................................................................. 139

Non-Small Cell Carcinoma ............................................................... 139
  Neoadjuvant Chemotherapy ......................................................... 139
  Adjuvant Chemotherapy .............................................................. 139
  Combined Chemoradiation ......................................................... 140
  Palliative chemotherapy .............................................................. 140
# List of Contributors

<table>
<thead>
<tr>
<th>Topic</th>
<th>Name /s</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>North of England Cancer Network</td>
<td>A Bassom, S Cooper</td>
<td>7</td>
</tr>
<tr>
<td>Terms of Reference, Introduction, Screening, Public Health and Prevention</td>
<td>D N Leitch</td>
<td>8-13</td>
</tr>
<tr>
<td>Referral Guidelines for Suspected Cancer</td>
<td>D N Leitch</td>
<td>14-19</td>
</tr>
<tr>
<td>Hospital Investigations</td>
<td>D N Leitch, L Mitchell</td>
<td>20-26</td>
</tr>
<tr>
<td>Multidisciplinary Teams</td>
<td>D N Leitch</td>
<td>27-29</td>
</tr>
<tr>
<td>Communicating the Diagnosis</td>
<td>D N Leitch</td>
<td>30-37</td>
</tr>
<tr>
<td>Informing the Primary Care Team, Specialist Nursing</td>
<td>D N Leitch</td>
<td>38-40</td>
</tr>
<tr>
<td>Clinical Trials</td>
<td>H Boal, B Workman, C Peedell, A Hughes</td>
<td>41-43</td>
</tr>
<tr>
<td>Audit, Cancer Waiting Times</td>
<td>J Brown</td>
<td>44-46</td>
</tr>
<tr>
<td>Treatment General Principles</td>
<td>D N Leitch</td>
<td>47-48</td>
</tr>
<tr>
<td>Surgery</td>
<td>S Barnard</td>
<td>49-51</td>
</tr>
<tr>
<td>Non Surgical Management of Lung Cancer</td>
<td>C Peedell</td>
<td>52-64</td>
</tr>
<tr>
<td>Malignant Mesothelioma</td>
<td>D N Leitch</td>
<td>65-75</td>
</tr>
<tr>
<td>Thymic Tumours</td>
<td>C Peedell, A Foden, J Ferguson, B Arivalagan</td>
<td>76-87</td>
</tr>
<tr>
<td>Referral Guidelines</td>
<td>D N Leitch</td>
<td>88</td>
</tr>
<tr>
<td>Sources of Information and Patients Support Groups</td>
<td>J Draffan</td>
<td>89-90</td>
</tr>
<tr>
<td>Continuing Care</td>
<td>J Draffan, T Peel</td>
<td>91-92</td>
</tr>
<tr>
<td>Supportive and Palliative Care</td>
<td>J Draffan, T Peel, Palliative Care NSSG</td>
<td>93-97</td>
</tr>
<tr>
<td>Pathology Guidelines</td>
<td>F Black</td>
<td>102-110</td>
</tr>
<tr>
<td>General References</td>
<td>D N Leitch</td>
<td>111-112</td>
</tr>
<tr>
<td>Appendix 1</td>
<td>L Mitchell</td>
<td>113-117</td>
</tr>
</tbody>
</table>
North of England Cancer Network

The North of England Cancer Network (NECN) was formed in January 2007 and covers a population of just over 3 million service users. The NECN was established when the longstanding organisations, Northern Cancer Network and Cancer Care Alliance merged. The NECN oversees cancer services and encompasses 9 Acute Trusts, 5 Primary Care Organisations, several Hospices/Specialist Palliative Care services and spans 2 Strategic Health Authority areas.

Cancer networks have been a feature of the health community for 10 years.

The focus for the Network is to achieve high quality outcomes for cancer patients and to look at equitable access of treatments and care.
Terms of Reference

- These guidelines have been written by various members of the North of England Cancer Network Executive Committee. These guidelines update, have combined and have largely drawn from the previous Cancer Care Alliance guidelines which covered the Southern part of the Northern Region and the Northern Cancer Network guidelines which covered the Northern part of the Region. The guidelines have been circulated to all members of the lung cancer group within the Northern Region for comment before publication. Grateful thanks go to those members who contributed to the guidelines and who reviewed and checked the text.

- It should be noted that these are guidelines and not policy, and that across the region there may be some variation according to local arrangements. The guidelines have been compiled with reference to several national documents as detailed in the references but in particular the relevant National Institute for Clinical Excellence Lung Cancer Referral and Lung Cancer Diagnosis and Treatment Guidelines (NICE, 2005a; NICE, 2005b) and the “Lung Cancer The diagnosis and treatment of lung cancer”, NICE clinical guideline 121, April 2011
Introduction

Incidence

- Excluding non-melanoma skin cancer, the four commonest types of cancer are breast, lung, colorectal and prostate cancer and these four cancers account for over 50% of all new cases (CRUK, 2008c).

- Worldwide lung cancer is the most common cancer. In the UK breast cancer is overall currently the most common cancer despite it being rare in men. The second commonest cancer overall is lung cancer. Until the late 1990’s lung cancer was the most common cancer in the UK.

- In men, lung cancer is the second commonest cancer after prostate cancer. In women, lung cancer is the second most common cancer after breast.

- Lung cancer accounts for approximately 1 in 7 of new cancer cases with about 38,000 (22,000 men, 16,000 women) cases/yr in UK with a crude incidence rate of 76.9/100,000 population in UK (CRUK, 2008d).

- Lung cancer is rare under the age of 40 years with 85% of cases occurring in those over the age of 60 years. The male:female ratio used to be 6:1 in the 1950’s but with changes in smoking habit the ratio is now 1.4:1.

- There are two main types of lung cancer: small cell lung cancer accounts for about 20% of cases, and non small cell lung cancer for 80% of cases. Adenocarcinoma is the most common type in non-smokers.

- There is a clear geographic variation with a high incidence in Northern England. Lung cancer is also strongly associated with social deprivation.

- Overall rates have fallen by more than 40% since a peak in 1970’s due mainly to a fall in smoking rates in men. Between 1995 and 2004 the incidence of
lung cancer in males fell by 23% whilst the incidence in women remained fairly static.

Mortality

- Despite the figures for incidence, lung cancer is the most common cause of death from cancer for men and women in the UK accounting for 24% of all male cancer deaths and 19% of all female cancer deaths.

- Lung cancer accounts for 6% of all deaths in UK and 22% of all cancer deaths in UK. There is a life time risk of lung cancer in men of 1in14 and in women of 1in17.

- For men lung cancer mortality rates fell steadily between 1992 and 2005 whilst over the same period the rates for women increased until the late 1990’s and then have levelled off (CRUK, 2008e).

Survival

- Over two thirds of patients are diagnosed at a late stage when curative treatment is not possible. It is hoped that measures to improve this will make a significant difference to survival rates. Many patients have significant co-morbidity (CRUK, 2008b).

- At present about 27% (15% in 1975) of men diagnosed with lung cancer are alive at 1 year and 30% (13% in 1975) of women with lung cancer are alive at one year with 7% of men alive at 5 years and 9% of women alive at 5 years. There is a variation in survival rates within UK but even the best areas have survival rates which are well below the European and USA rates. In the USA five year survival rates are 13% for men and 17% for women.

- To address some of these differences and to try to collect national data a national lung cancer audit programme has been launched (LUCADA) (Reference). In addition there is a National Awareness and Early Diagnosis
Initiative (NAEDI) to try to diagnose lung cancer earlier and thereby improve outcome.

**Risk Factors**

- Smoking is by far and away the most significant risk factor for lung cancer. Approximately 90% of lung cancers in men and 83% of lung cancers in women are estimated to be due to smoking (CRUK, 2008a).

- In the UK about 25% of all adults aged >16 years smoke (11 million people). In children <1% of 11 and 12 year olds smoke but this figure rises to 20% of 15 year olds.

- Life long current smokers are 15x more likely to die from lung cancer than life long non-smokers. The duration and the level of consumption are related to the risk of lung cancer. Compared with non smokers, for smokers of 1-14/day the risk of dying from lung cancer is 8x, and for those who smoke 25+/day the risk is 25x. Duration is however more significant than level of consumption. The risk of 20/day for 20 years may be more than 16x as hazardous as 20/day for 10 years. The earlier smoking starts the greater the danger.

- Smoking cessation has significant health benefits at whatever age and is to be strongly recommended. A lifelong male smoker has a risk of 15.9% for developing lung cancer by 75 years, but stopping at 60, 50, 40 and 30 years reduces this risk to 9.9%, 6.0%, 3.0% and 1.7%. Similar figures apply to women with a life time risk of lung cancer to age 75 years for smokers of 9.5%. Stopping smoking before middle age avoids the majority of the risk for lung cancer. A lifelong never smoker has a risk of 0.5% of developing lung cancer by 75 years.

- A further risk factor is radon gas which naturally occurs, and in some areas, can accumulate in houses. It may account for 9% of lung cancers in some circumstances. Other risk factors include industrial carcinogens including arsenic and some hydrocarbons and asbestos.
• A family history of a first degree relative with lung cancer is associated with a 2x increased risk independent of smoking, especially if the cancer was diagnosed at an early age. Previous treatment for cancers such as lymphoma is also a risk factor which can be present up to 30 years later.

Screening

• At present there is no proven effective screening test for lung cancer. Several large studies, using various combinations of x-ray and sputum cytology, have failed to show any clinically significant benefit. Trials looking at CT screening have been completed and further trials are under way.

• The Network welcomes the pledge in the Cancer Reform Strategy to commission research on the feasibility of a UK trial of CT screening for lung cancer, working with the National Cancer Research Institute (DH, 2007).
Public Health and Prevention

The Network fully supports the drive to improve cancer care and services throughout the United Kingdom. In particular for England, the Network supports the NHS Cancer Plan (DH, 2000) and the NHS Cancer Reform Strategy (DH, 2007) and the NAEDI around lung cancer.

The Network supports the aims of the Cancer Reform Strategy to promote good Public Health and help to prevent cancer through improved awareness of risk factors and adoption of healthier lifestyles. In particular the Network supports the Cancer Reform Strategy drive to reduce smoking.

It is recommended that the Network and all individual units support all national and local anti-smoking measures wherever possible.

It is strongly recommended that the Network support measures taken to try to prevent / reduce school children starting to smoke and to help them to stop smoking.

At the individual level health workers should enquire into smoking behaviour, emphasise the importance of stopping smoking and offer encouragement and support. All measures available to help stop smoking should be considered and made available wherever possible.

The Network supports the aims stated in the Cancer Reform Strategy to raise public awareness of cancer and the planned national audit in primary care of newly diagnosed cancers and the NAEDI around lung cancer throughout the UK.

The Network and the Lung NSSG take note of the recommendation in the 2011 NICE guidance that “The public needs to be better informed of the symptoms and signs that are characteristic of lung cancer, through coordinated campaigning to raise awareness”.

Referral Guidelines for Suspected Lung Cancer

General Principles

- Lung cancer can present in a vast number of ways and a high index of suspicion should be held especially when treating those most at risk – long term smokers. It is recommended that General Practitioners, but also all hospital Consultants and those treating patients, should follow the national recommendations regarding referral. These NICE guidelines are summarised here (NICE, 2005b, NICE clinical guideline 121, 2011).
<table>
<thead>
<tr>
<th>CCG Referral Pathways</th>
<th>CCG Population*</th>
<th>Hospital</th>
<th>Designated MDT</th>
<th>Named Lead/Contact/Tel/Fax</th>
<th>Centres for Surgery</th>
</tr>
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<td>Gateshead Health NHS FT</td>
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<tr>
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<td>275.3</td>
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<td></td>
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<td>South Tyneside District Hospital</td>
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<tr>
<td>South Tyneside</td>
<td>148.2</td>
<td>South Tyneside NHS FT</td>
<td>University Hospital of North Durham</td>
<td>Dr N Munro T:0191 3332309 F:0191 3332884</td>
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<td>Cumberland Infirmary</td>
<td>Dr P Plant T:01228 814142 F:01228 814819</td>
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Source - CCG populations based on 2011 Census Populations
Patient Centred Care

- People being referred for suspected cancer should have the opportunity to make informed decisions about their care and treatment taking into account individual needs and preferences.

- Good communication is essential between healthcare professionals and patients with the provision of suitable evidence based information. The Network and the Lung NSSG take note of the NICE Guidance that “A lung cancer clinical nurse specialist is available at all stages of care to support patients and carers”.

- Unless excluded by the patient, carers and relatives should have the opportunity to be involved.

Making a diagnosis

- Primary health care professionals should be familiar with typical presenting features of lung cancer and be alert to the possibility of lung cancer when there are unusual symptoms or where there is failure to improve from what is thought to be a benign condition. Discussion with a specialist should be considered if there is uncertainty.

- If diagnosis or referral has been delayed the patient should be offered the opportunity to see another healthcare practitioner.

Investigations

- Investigations in primary care should not delay referral where cancer is suspected.

The need for support and information

- Following referral the primary health care professional should assess the patient need for continuing support whilst awaiting their appointment noting that some patients may find the referral for suspected cancer particularly difficult and that both men and women may
need support but display their need differently. Cultural differences should also be considered with appropriate action as necessary.

- Information given should include:
  - Where the patient is being referred
  - How long they will wait for an appointment
  - How to obtain further information about the suspected cancer
  - Who they will see
  - What to expect
  - What type of tests might be carried out
  - How long it will take to get a diagnosis.

- Patients being referred should normally be told that they are being referred to a cancer service.

**Continuing education**

Primary health care professionals should take part in education, peer review and other activities to improve or maintain clinical consulting, reasoning and diagnostic skills, and communication skills. Such awareness and understanding around lung cancer is important to earlier diagnosis and improved outcome.
Referrals

- There should be arrangements in place to ensure that letters about non-urgent referrals are seen by a specialist so that a change in priority can be made if needed.

- There should be local arrangements in place to ensure a maximum wait for non-urgent referrals in accordance with national targets and recommendations.

- There should be arrangements in pace to ensure that those who miss their appointments are identified so that they can be followed up.

- When making a referral the healthcare practitioner should use local referral pro formas when these are in use and include all relevant details.

- When a decision to refer has been made the healthcare practitioner should make the referral within 1 working day.

Specific Guidelines for Urgent Referral for Suspected Lung Cancer

- Definition: Urgent: The patient is seen within the national target for urgent referrals (currently 2 weeks). The following recommendations are those identified in the relevant NICE guideline (NICE, 2005b, NICE Clinical Guideline 121, 2011):

General

- A patient with symptoms suggestive of lung cancer should be referred to a member of a team specialising in the management of lung cancer. Very often this will initially be a respiratory physician.
Specific – Referral for Chest X-ray

- An urgent referral for a chest X-ray should be made when a patient presents with:
  - Haemoptysis or
  - Any of the following unexplained persistent (> 3 weeks) symptoms or signs
    - Cough
    - Chest and or shoulder pain
    - Dyspnoea
    - Weight loss
    - Chest signs
    - Hoarseness
    - Finger clubbing
    - Cervical or supraclavicular lymphadenopathy
    - Features suggestive of a metastasis from lung cancer (eg brain, bone, liver or skin).

- In addition, investigations should be arranged for those with chronic lung disease where there is a change in symptom complex e.g. changed cough in COPD / fibrosis.

- A report should be made to the primary healthcare professionals within 5 days of the referral for a chest X-ray.

- Where a CXR has been requested in primary or secondary care and is incidentally suggestive of lung cancer, a second copy of the radiologist’s report should be sent to a designated member of the lung cancer MDT, usually the chest physician. The MDT should have a mechanism in place to follow up these reports to enable the patient’s GP to have a management plan in place.
Specific - Referral to a Lung Cancer Unit

- An urgent referral should be made for either of the following:
  - Persistent haemoptysis in smokers or ex-smokers who are aged 40 years or older
  - A chest X-ray is suggestive of lung cancer (including pleural effusion and slow to resolve consolidation).

- In addition to these NICE recommendations it should also be noted that a CXR may be normal despite the presence of cancer and where there is clinical suspicion then a normal CXR should not be taken as false reassurance.

- Where there is suspicion of lung cancer a referral should be made even with a normal CXR.

- A referral should be made while awaiting the result of a CXR if any of the following are present:
  - Superior vena cava obstruction
  - Stridor
  - As clinical circumstances indicate
  - As indicated above in smokers and ex-smokers over 40 years who have persistent haemoptysis.

- Note a proportion of patient with lung cancer present as acute medical emergencies.

- In general a high index of suspicion should be held for those with particular risk factors although lung cancer can present in any patient with or without a risk factor. Risk factors include:
  - Current or ex smokers
  - Those with COPD
  - Previous asbestos exposure
  - Previous Cancer
NSSG GUIDELINES FOR TEENAGE AND YOUNG ADULTS

Teenage and Young Adults Peer Review Measures Topic 11-1C (Functions of the Network Site Specific Groups for TYA)

1. Teenage and Young Adult Pathway for initial Management
   The NSSG has received the document named ‘NECN Teenage and Young Adult Cancer Pathway Guidance Paper’ and agrees to follow the generic TYA Pathway with any site specific variations to be documented. Please see Appendix 1 for pathway.

2. Teenage and Young Adult Pathway for Follow up on completion of first line treatment
   Patients aged 19-24 years will adopt the site specific adult follow up pathway on completion of first line treatment. It is acknowledged by both the CYPCG and NSSGs across NECN that further work is required to develop these pathways for this age group and partly in response a TYA working group has been established to take this work forward.
   If advice is required regarding the follow up care of a 19-24 year old patient, then the Lead TYA Clinician at the designated hospital or PTC should be contacted. Please see Appendix 2 for contact details.
   Patients age 16-18 years will continue to adopt the paediatric and adolescent follow up protocol of the PTC and all advice should be sought direct from the On Call Paediatric Oncologist at Royal Victoria Infirmary 0191 2336161. Paediatric Follow Up Protocols can be found on the CCLG website (2005 second edition) with the exception of trial specific protocols which can be requested via the Children’s Trial Co-ordinator based at the RVI.

3. Pathways for cases involving Specialised NHS services (Only Gynae and Sarcoma)
   The Gynae NSSG and SAG reviewed and agreed the Specialised NHS Service pathway for patient’s age 16-24 years. This is attached in Appendix 3
Appendix 1 – Teenage and Young Adult Pathway for initial Management

Teenage and Young Adult Cancer Pathway – 19 to 24 years old

- If patient is aged between 0 – 18 year see Children’s pathway

* Patients who decline treatment at the PTC or TYA designated hospital will have their MDT discussion within the local tumour site specific MDT and TYA MDT

Holistic assessment and rehabilitation consideration
Inform patient’s GP
Appoint Key Worker

Max Time in days

Urgent referral made by GP/0GP.Screening

Access as per local Tumour Site Specific protocol:
- Site specific diagnostic investigations
- May include diagnostic biopsies, but not definitive cancer surgery

Cancer diagnosis or highly suspicious Patient informed of joint MDT review and place of care options
NB MDT discussion should take place in tumour site specific MDT within PTC/TYA designated hospital AND TYA MDT

Review at TYA MDT

Communication & liaison between MDTs

Review at PTC/TYA DH Site Specific haematology-oncology/solid tumour MDT.

Joint treatment planning decision agreed, including:
- Diagnosis and treatment modalities/ regimens
- Place of treatment delivery, depending on patient age:
  - > 16-18 years - PTC facility only (Paediatric & Adolescent Oncology, Ry, Newcastle)
  - > 19-24 years – choice of PTC facility (Adult Oncology, FH, Newcastle) or TYA designated hospital
- Named consultant in charge of each treatment modality
- The arrangements/referrals to provide age appropriate support if the treatment is delivered outside the PTC facility
- The results of the discussion of fertility issues
- Consider entry into clinical trials
- Consider palliative & supportive care needs
- Identify patient’s key worker

First treatment

PTC (RVI or Freeman) – treatment and ongoing care (with options for shared care or supportive care)

Designated TYA hospital treatment with option of TYA MDT outreach support 19–24 yr

Haematological/Onological Treatment
- First definitive treatment
- Surgery
- Chemotherapy
- Biological therapy
- Radiotherapy

Assess response at site specific haematology-oncology/solid tumour MDT

Consider need for further/consolidation treatment

Relapse or recurrent disease

No

Long term follow up protocol

Further Treatment

 Palliative Care

Abbreviations
- TYA (Teenage and Young Adults)
- TYA DH (Teenage and Young Adult Designated Hospitals)
- PTC (Principal Treatment Centre Newcastle upon Tyne hospitals)

TYA Cancer Ideal Pathway Map version 1.7
BL/RS/BU/T and acknowledgement to West Cancer Network
## Appendix 2 – Contact Details

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<tr>
<th>Name of NHS Trust and designated hospital site</th>
<th>Name of MDT</th>
<th>TYA Lead Clinician</th>
<th>TYA Lead Nurse</th>
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<tr>
<td><strong>Principal Treatment Centre</strong></td>
<td>All MDTs:</td>
<td>Dr Emma Lethbridge</td>
<td>Suzanne Brand</td>
<td>0191 2138464</td>
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<td>Specialist Gynaecology</td>
<td>Ms Christine Ang</td>
<td>Alison Guest</td>
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<tr>
<td><strong>City Hospitals Sunderland NHS Foundation Trust - at Sunderland Royal Hospital</strong></td>
<td>Specialist Urology (Testicular only)</td>
<td>Dr Scott Marshall</td>
<td>Faye Laverick</td>
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<td>Dr Dianne Plews</td>
<td>Jill Linton</td>
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<td>All MDTs:</td>
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<td>VACANT</td>
<td>01228 523444</td>
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Appendix 3 – NHS Specialised Services Pathway

NHS Specialised Services - Referral Pathway for Primary Malignant Bone Cancer for patients age 16-24 years within the North of England

Paediatrician

GP

Radiology/Incidental Finding

Referral to Sarcoma Service at Freeman Hospital, Newcastle (FRH)
See Sarcoma pathway for contact details

If age 16-18 years refer to PTC paediatric & adolescent MDT at RVI and Bone & Soft Tissue MDT at FRH

All patients to be discussed at the TYA MDT (see TYA pathway for contact details)

If age 19-24 years refer to Bone & Soft Tissue MDT at FRH

Necessary to refer to National Ewing's Sarcoma MDT for discussion?

Yes

Submit electronic MDT proforma and link in via WebEx.

Please see Bone & Soft tissue site specific pathway and/or paediatric & adolescent pathway for detail

5 years post treatment for patients age 16-24 years

No

Please see Bone & Soft tissue site specific pathway and/or paediatric & adolescent pathway for detail

Age 16-18 at time of diagnosis refer to long term follow up clinic/MDT

Age 19-24 yrs at time of diagnosis follow up on adult protocol

Primary Bone Cancer Pathway DRAFT
Toni Hunt NECN Version 0.3 Aug 2012

27
Hospital Investigations

General Principles

- These guidelines are based on the NICE Lung Cancer guidelines. All those involved in the management of patients with lung cancer should be familiar with these guidelines (NICE, 2005a, NICE Clinical Guideline 121, 2011). The main points are summarised here with local recommendations.

- Local arrangements should be put in place to ensure that patients referred urgently are seen within the agreed national target (currently 2 weeks).

- Patients with suspected lung cancer who are identified by another hospital team or by chance, should be referred urgently to a member of the lung cancer team – usually a respiratory physician.

- Such referrals should be made within 1 working day of the decision to refer and the referral faxed to the receiving consultant. Such referrals should also be followed up with a telephone call to the respiratory physician to ensure that the referral has been received. Local arrangements may differ including the receipt of referral in a central 2 week rule booking office but the same principles should be followed.

- On receipt of referral from another hospital team then the respiratory physician should mark the referral as urgent (2 week rule) if an out patient appointment is requested and the patient should be seen as such and managed on the 62 day pathway. If an in patient referral is received then the patient should be seen as soon as possible and ideally within 2 working days.

- All lung cancer teams should be aware of the national targets for the diagnosis and management of lung cancer and work towards locally agreed pathways to promote patient care such that all patients are seen, diagnosed and treatment started with 62 days if the patient wishes.
• If a CXR has been performed and an incidental suspected cancer identified then a second copy of the radiologist’s report should be sent to a designated member of the Multidisciplinary team (MDT) usually the respiratory physician.

• The MDT should have a mechanism to ensure that there is follow up of these reports to ensure a management plan has been instituted by the patient’s GP.

Specific Considerations

• Only half of patients referred to a clinic with suspected lung cancer will turn out to have this pathology. Investigation therefore has diagnostic and staging goals. In order to prevent unnecessary delay these may be combined but care should be taken to ensure that the pathway is tailored to the individual patient to minimise unnecessary investigations. CT imparts a significant radiation dose and contrast has a small but significant morbidity and mortality.

• If the chest x-ray shows a mass a combined diagnostic/staging scan should be performed including the liver and adrenals (see below). If however there is no definite evidence of cancer, e.g. normal chest x-ray, a CT scan of the chest alone may be sufficient to exclude or confirm a lesion. Contrast is not usually necessary but may be used if there is uncertainty or the Radiologist is not confident reporting non-contrast scans. If the chest scan shows a lesion a full staging scan should be performed at the same attendance. If contrast has been given the liver and adrenal phase may be set up before the chest scan so the scan can be continued immediately.

• It is recognised that in some units a Radiologist is not always present when the scan is performed and the decision to do a diagnostic study or combined diagnostic and staging scan will need to be made at the time of protocolisation.

• When a patient with known or suspected lung cancer is seen in the clinic then they should be offered a contrast enhanced CT as an initial investigation to
further the diagnosis and stage the possible disease. This should include the liver and adrenal glands.

- Local consideration should be made to specific arrangements in the investigation pathway such that the results of CT are available before deciding on the most appropriate next management step. For example, pre-arranged CT slots shortly after an initial clinic visit with rapid review of the patient. For example, CT before a clinic appointment provided this does not lead to unnecessary CT scans or delay in referral. Where there is a CT scan before a clinic appointment then there should be appropriate discussion with the patient.

Rapid Access Lung Clinics
- Rapid access clinics should be provided where possible for the investigation of patients with suspected lung cancer, because they are associated with faster diagnosis and less patient anxiety.

- Local arrangements should be in place with consideration given to concurrent investigation of suspected abnormalities such that tests are done in parallel rather in series. E.g. A patient with a potentially operable lung cancer might have CT biopsy and FDG-PET requested in parallel.

- With regard to the investigation of lung cancer it is important to identify cell type and stage wherever possible in order to identify the most appropriate management.

Sequence of Investigations
- Choose investigations that give the most information about diagnosis and staging with least risk to the patient. Think carefully before performing a test that gives only diagnostic pathology when information on staging is also needed to guide treatment.

- Chest CT should be performed before:
- An intended fibreoptic bronchoscopy
- Most other biopsy procedures

Peripheral Primary Tumour

- Offer CT or ultrasound guided transthoracic needle biopsy to patients with peripheral lung lesions when treatment can be planned on the basis of this test.
- Biopsy any enlarged mediastinal nodes (>10mm maximum short axis on CT) or other lesions in preference to the primary lesion if determination of stage affects treatment

Central Primary Tumour

- Offer fibreoptic bronchoscopy to patients with central lesions on CT where nodal staging does not influence treatment. Enlarged lymph nodes (>10mm maximum short axis on CT) may be simultaneously sampled with TBNA (non-ultrasound guided) if required for diagnosis.

Mediastinal Lymph Node Assessment

- Offer PET-CT as the preferred first test after CT showing a low probability of mediastinal malignancy (lymph nodes <10 mm maximum short axis on CT) for patients who are potentially suitable for treatment with curative intent.
- Offer PET-CT, or EBUS guided TBNA, or EUS guided FNA, or non ultrasound guided TBNA as the first tests for patients with an intermediate probability of mediastinal malignancy (lymph nodes between 10-20mm maximum short axis on CT) who are potentially suitable for treatment with curative intent.
- Offer neck ultrasound with sampling of visible lymph nodes or non-ultrasound guided TBNA to patients with a high probability of mediastinal malignancy (lymph nodes >20mm maximum short axis on CT). If neck ultrasound is negative, follow with non ultrasound guided TBNA, EBUS-TBNA or EUS guided FNA. If non ultrasound guided TBNA is negative follow with EBUS-TBNA or EUS guided FNA.
- Offer neck ultrasound with biopsy of visible lymph nodes to patients that have neck nodes detected by initial CT. If negative follow with non-ultrasound guided TBNA or EBUS-TBNA or EUS guided FNA.
- Evaluate PET-CT positive mediastinal nodes by mediastinal sampling (except where there is definite distant metastatic disease or a high probability that N2/N3 disease is metastatic (for example, if there is a chain of lymph nodes with high FDG uptake).
- Consider EBUS and EUS for initial staging of the mediastinum as an alternative to surgical staging.
- Confirm negative results obtained by non—ultrasound guided TBNA using EBUS-TBNA, EUS guided FNA or surgical staging.
- Confirm negative results obtained by EBUS-TBNA and or EUS guided FNA using surgical staging if clinical suspicion of mediastinal malignancy is high.

Stage M1b
- Where metastatic disease is considered then CT, radiography, bone scan or MRI should be requested as necessary. Confirm the presence of isolated distant metastases / synchronous tumours by biopsy or further imaging (for example MRI or PET-CT) in patients being considered for treatment with curative intent.
- Consider MRI or CT of the head in patients selected for treatment with curative intent, especially in stage III disease.
- Offer patients with features suggestive of intracranial pathology CT of the head followed by MRI if normal, or MRI as an initial test.
- An X-ray should be performed in the first instance for patients with localised signs of symptoms of bone metastases. If the results are negative or inconclusive, either a bone scan or an MRI should be offered.
- Avoid bone scintigraphy when PET—CT has not shown any bone metastases.
- Sputum cytology is rarely indicated and should be reserved for the investigation of patients who have centrally placed nodules or masses and are unable to tolerate, or unwilling to undergo, bronchoscopy or other invasive tests.
- Ensure all patients potentially suitable for treatment with curative intent are offered PET-CT before treatment.
• The Cancer Network should have a system of rapid access to PET-CT for eligible patients.

**Staging**

With regard to staging the NICE guidelines recommend the following:

**Non Small Cell Lung Cancer**

• CT of the chest and abdomen is the investigation of choice to stage the primary tumour and to detect metastatic disease. Post contrast CT of the brain should be included in the initial staging if symptoms are present or if curative therapy, including surgery, radiotherapy, chemotherapy or a combination, is being considered. If any such patient has not had a head scan at the initial staging it should be performed separately before treatment. MRI is the investigation of choice if the CT is normal in the presence of neurological signs.

• Staging CT should include post-contrast scans through the chest (to include supraclavicular fossae) and upper abdomen (to include liver and adrenal glands). 100-150mls of intravenous iodinated contrast should be injected at 3-4ml/sec. The chest should be scanned during the arterial phase (20-30 sec delay), and the abdomen during the portal venous phase (60-70 sec delay).

• In the assessment of mediastinal and chest wall invasion:
  - CT alone may not be reliable
  - Other techniques such as ultrasound should be considered where there is doubt
  - Surgical assessment may be necessary if there are no contraindications to resection.

• Pancoast (superior sulcus) tumours are best visualised by multiplanar reconstructions, however the extent of these tumours is best demonstrated by MRI.
• All patients potentially suitable for treatment with curative intent should be offered PET-CT.

• Patients identified as N0 or N1 disease with M0 on CT and FDG-PET should proceed with surgery without further histological/cytological confirmation of lymph nodes.

• Where enlarged N2/N3 nodes are seen on CT but are negative on FDG-PET, it must be realised that FDG-PET has a false negative rate and biopsy should be undertaken, especially if the primary tumour has a low SUV.

• Clearly where there is any doubt then there should be MDT discussion and a fully informed discussion of the results and possible options with the patient.
Small Cell Lung Cancer

- The initial presentation of Small Cell Lung cancer (SCLC) is usually similar to that of all kinds of Lung Cancer except that progression is usually more rapid and Superior Vena Caval Obstruction is more common.
- Therefore the initial investigations will be the same as in the general imaging guidelines.
- The basics of additional Staging and follow up are also similar. Surgery is not normally a treatment option except in very limited disease.
- Specific variations in Imaging for Small Cell Lung Cancer are given below.

A. STAGING

- As with Non Small Cell Lung Cancer, CT of the chest and abdomen is the investigation of choice to stage the primary tumour and to detect metastatic disease.
- Post contrast CT of the brain should be included in the initial staging if symptoms are present or if localised therapy, including surgery or radiotherapy, usually in combination with chemotherapy, is being considered.
- If any such patient has not had a head scan at the initial staging it should be performed separately before treatment.
- MRI is the investigation of choice if the CT is normal in the presence of neurological signs.
- CT may not provide complete staging and other techniques e.g. ultrasound, with or without contrast, may be considered.
- An 18F-deoxyglucose positron emission tomography CT (FDG PET-CT) scan should be performed to stage disease in any patient who at diagnosis or after down staging is to be offered surgery or radiotherapy for other than local palliation.
B. Follow-up

- If response to treatment such as chemotherapy cannot be assessed adequately by CXR repeat CT scans may be required during the course of treatment.
- At the end of a treatment programme repeat staging may be necessary to plan further management.
- If the patient develops new or recurrent symptoms targeted imaging should be performed. Formal restaging may also be required.
- If PET-CT is used to assess residual disease then a gap of at least 6 weeks should be left after chemotherapy.
Multidisciplinary teams

- All patients with a working diagnosis of lung cancer should be discussed at the cancer unit MDT. The multidisciplinary team is now an established part of the management of patients with cancer.

- The MDT should be set up in accordance with the Manual of Cancer Standards (DH, 2004). Each cancer unit has been assessed as part of the Cancer Services Peer Review assessment exercise in recent years and the standards described should be regularly reviewed and understood by each cancer unit.

- In particular within each unit there should be a local lung cancer lead. This lead and the MDT as a whole should:

  - Ensure that designated core members at the meeting work effectively, in teams and that decisions regarding all aspects of diagnosis, treatment and care of patients, and decisions regarding operational policies, are true multi-disciplinary decisions.

  - Ensure that care is given accordingly to recognised guidelines with appropriate information being collected to inform clinical decision-making and to support clinical governance / audit.

  - Ensure that mechanisms are in place to support the entry of eligible patients into clinical trials, subject to the patient giving fully informed consent. The MDT should record the reasons for patients not being entered in to trials that are open.

  - Each unit should have a team of members of the different disciplines involved in the investigation and management of lung cancer. This group should meet regularly most likely weekly but at least every two weeks, and attendance records kept. The core members should be:
- Respiratory physician with an interest in lung cancer
- Clinical and/or Medical Oncologist
- Radiologist
- Histopathologist/Cytologist
- Thoracic surgeon
- Lung cancer nurse specialist
- Palliative care representative
- MDT Coordinator /Tracker.

- Each newly diagnosed patient should be discussed by the group and plans made for further investigation and treatment.

- Decisions should be recorded for each patient. It is recommended that each unit determine its preferred mechanism for recording the treatment plan for each patient at the MDT but an example of good practice might include a summary sheet of all the key data items and the management plan with brief explanation of key reasoning which could be filed in the patient’s case notes.

- The group should have an operational policy, mutually agreed and reviewed at an annual meeting.

- It is recommended that each cancer unit establish a robust system for prospective data collection in order to allow for clinical audit. It is recommended that each unit should collect data in accordance with the National Clinical Lung Cancer Audit (LUCADA, 2007).

- It is recommended that each cancer unit is familiar with the LUCADA reports and generates appropriate action plans in line with the key recommendations identified from the reports.

- In particular with regard to LUCADA each unit must strive to:
  - Submit data for 100% of cases
- Collect data for the key casemix variables stage, performance status and co-morbidity
- Note that histological and cytological confirmation rate is considered in the LUCADA report as a marker for quality of care
- Be aware of their own anti-cancer treatment rates in comparison with the national average.
Communicating the diagnosis

General Considerations

- The guidelines described here draw on guidance published by the British Thoracic Society (BTS, 2008) and the NICE Clinical Guideline 121, 2011.

- Find out what the patient knows about their condition without assuming a level of knowledge. Provide patients with the opportunity to discuss tests and treatment options in private environment, with the support of carers and time to make an informed choice.

- Ensure that a lung cancer clinical nurse specialist is available at all stages of care to support patients and carers.

- Offer accurate and easy to understand information to patients and their carers. Explain the tests and treatment options, including potential survival benefits, side effects and effect on symptoms.

- Consider tailor-made decision aids to help patients to:
  - Understand the probable outcomes of treatment options
  - Consider the personal value they place on benefits versus harms of treatment options
  - Feel supported in decision making
  - Move through the steps towards making
  - Take part in decisions about their healthcare

- Offer patients a record of all discussions that have taken place with them and a copy of any correspondence with other healthcare professionals. Ensure all communications are worded in such a way to assist understanding.

- Respect the patient’s choice if they do not wish to confront future issues.
• Avoid giving patients unexpected bad news by letter. Only give unexpected bad news by phone in exceptional circumstances.

• Offer to discuss end-of-life care with the patient sensitively and when appropriate. Wherever possible avoid leaving this discussion until the terminal stages of the illness.

• Document decisions about the patient and end of life care. In particular document:
  o Specific concerns of the patient
  o Their understanding of their illness and its prognosis
  o Important values or personal goals for care.
  o Their preferences for the types of care or treatment that may be beneficial in the future and their availability.

• Share information between healthcare professionals about:
  o Any problems the patient has
  o The management plan
  o What the patient has been told
  o What the patient has understood (where possible)
  o The involvement of other agencies
  o Any advance decision made by the patient.

• Each unit should have a policy on the breaking of bad news. This should be discussed and agreed with patient representatives, and steps made to disseminate and use it throughout the unit. The points raised should include the following:

• Information should be given where possible in privacy, in comfortable surroundings and with no interruptions from phone or personnel. Where this is impossible because the patient is bed-bound and cannot be moved, every effort should be made to respect the patient’s privacy by ensuring
the other patients’ relatives are not in the room, drawing the curtains round the bed, etc.

- The information should, where possible, be given by a consultant or senior member of the junior staff experienced or trained in the giving of bad news. In the event of the latter, the patient should have an opportunity to speak to the consultant as soon as possible afterwards.

- The person breaking the news should have as much information as possible about the patient’s condition, although circumstances may dictate that the news is broken before all such information is available.

- The patient should be given the opportunity to have a relative or friend present.

- A member of nursing staff, preferably either a Lung Cancer Nurse Specialist or a member of the team caring for the patient, should be present and remain after the doctor has left.

- The information should be given sensitively (slowly and gently) using patient feedback and body language to assess the pace of information needed at this time. Simple terminology should be used, avoiding medical terminology.

- The patient should be given adequate time to ask questions both of the doctor and of the nurse.

- Treatment options should be discussed, including those not possible and why.

- The patient should be given adequate information to take part in the decision making process. Some patients may not wish or be able to take in all such information at the first session, and may require further
discussion at a later date. Written information should be available to support the discussion and information regarding support groups should also be given at this time.

- The patient should receive a written plan outlining the proposed treatment and/or further investigations needed to decide on a plan of action. Wherever possible, the plan should include a date for the next step and an outline of the timescale for treatment.

- It should be made clear to the patient / relatives how to make contact with the team if questions arise after the consultation.

- The patient and family should have the opportunity to remain in privacy for a while after the interview if they need to do so. It is important to be sure that the patient or carer is in a fit state to drive home if applicable.

- The interview should be documented in the notes.

- It is imperative that those involved in a consultation around the diagnosis of lung cancer appreciate that this will often involve the delivery of bad news. It is vital that those who regularly break bad news to any cancer patient have appropriate training in communication skills. Fundamental frameworks exist in relation to the breaking of bad news and those involved should be familiar with such a framework. A recommended framework is described below:

**Framework of Discussion with Patients**

**A Framework for Breaking Bad News – A Six Step Guide**

**Step 1: Getting Started**

- Ensure you provide a suitable environment – privacy.
- Who does the patient want with them – this may not be the same as the people that are with them!
- Do you think it would be helpful to have a nurse sitting in to support the patient after the consultation?
- Allow time to do this.

**Step 2: Finding out how much the patient knows**

- Use open-ended questions (e.g. “It would help me to know what you understand about your illness so far”).
- Depending on their answers, check out the reasons why they have thought things (e.g. “Why have you thought that?”).

**Step 3: Finding out how much the patient wants to know**

- The objective is to get a clear invitation to share knowledge (e.g. “would you like me to explain that in more detail?” ”Would it help if you saw the X-rays?”
- If the patient expresses a preference not to discuss the information, leave the “door open” for later.

**Step 4: Sharing the information**

- Plan a basic agenda – diagnosis, treatment plan, prognosis, support. NOTE – it may not be appropriate to cover all of these.
- Start from the patient’s level – what they already know – and build on this.
- Give the information in small chunks.
- Might be helpful to use the narrative of events “You coughed up some blood, and then you had a CXR”.
- Give the patient a WARNING SHOT – “I’m afraid this is a serious condition.
- Allow time to evaluate the verbal and non-verbal response then give more details as required.
- If the patient asks direct questions you should answer directly, provided you are clear what they are asking. The terms tumour, cancer, benign and malignant are often confused and may need explaining.
- It is useful to help patients recall information afterwards to use drawings, diagrams.
- Listen to the patient’s agenda.
- Allow frequent pauses; check that they understand what you are saying at regular intervals.

**Step 5: Responding to the patients’ feelings**
- Pause to allow the news to sink in.
- Acknowledge any distress (empathy).
- Explore the reasons for the distress by using probing questions – but move on if this is too difficult for the patient.
- Elicit feelings.
- Explore any other concerns and prioritise these.

**Step 6: Planning and follow-through**
- Demonstrate understanding of the patient’s problem list.
- Make a plan / strategy and explain it (“prepare for the worst and hope for the best”).
- Identify the patient’s coping strategies and reinforce.
- Establish if they have other sources of support.
- Summarise and allow time for questions.
- Encourage them to write down questions for the next consultation.
When to provide information

- It must be recognised that the patient pathway does not necessarily fall into discrete steps (e.g. referral – diagnosis – treatment). Many patients will therefore require a wide range of information.

- Provide information at different times. Some may never want to know anything whereas others may require detailed data even before a diagnosis has been confirmed. It is therefore essential to establish what a patient already knows and what they wish to know.

Discussion about treatment options

- Although any member of the MDT may deliver the first indication of treatment options, it is often the respiratory physician who does this first.

- It is recommended that discussion is kept to a minimum if the patient is to see another specialist who will actually be delivering the treatment e.g. surgeon, oncologist in order to minimise any confusion.

- Some patients may require some information and in these circumstance the message should be kept clear, and ensure that the patient understands that the treating specialist may alter the exact plan nearer the time. Basic information that might be communicated to a patient can be found in the British Thoracic Society Guidelines on giving information to lung cancer patients (BTS, 2008).

- Any information given to the patient must be accurate. It is recommended that each unit agree on local basic statistics which should be given to patients regarding treatment options. The patient may need to see more than one specialist in order to make their decision.

- Information may be given in one visit but it should be noted that very often several visits may be needed or other delivery methods.
• Arrangements should be made in each unit locally to determine the best methods for ensuring accurate information is given and that the patient receives all the information required.

• Provision of information should be offered in a form that is tailored to the needs of the individual patient. The treatment, care and information provided should be culturally appropriate and in a form that is accessible to people who have additional needs such as people with physical, cognitive or sensory disabilities and people who do not read or speak English.

• Unless specifically excluded by the patient, carers and relatives should have the opportunity to be involved in the decisions about the patient’s care and treatment, although care should be taken to ensure that the patient is not sidelined in some circumstances.

• Careers and relatives should also be provided with the information and support that they need.

• Being Positive. It is important to endeavour to maintain hope by the provision of the diagnosis and a solid management strategy so that the patient feels supported. It is important not to say “there is nothing more that we can do.” It is recommended instead to say that further surgery, radiotherapy or chemotherapy is not an option but supportive and palliative care is always available. “We can help you although we cannot cure the condition.”

Prognosis

• Patients often ask “how long” without thinking clearly whether they are really ready for this level of information. Often little information is retained.
Information about prognosis is often a source of distress especially when mixed messages are given. It is recommended therefore that an assessment is made of exactly what the patient wants to know and why. If a figure is requested then emphasis that any figures are the average (median) and some patients do worse and some do better. Clearly document any information given.

Documentation

Since 2004 the Department of Health has recommended that all letters about patients should be copied to the patient unless there is an important reason not to. This can facilitate patient information and indicate to the patient what has been said to primary care, and indicate to primary care what has been said to the patient. Where letters are copied then the language used in such letters should be appropriate. It is recommended that locally agreed arrangements are put in place regarding this recommendation.

Survival Figures

The following figures in the table are given as general guideline figures which each unit may wish to consider.

Small cell lung cancer

<table>
<thead>
<tr>
<th></th>
<th>Limited Stage Disease</th>
<th>Extensive Stage Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Treatment</td>
<td>12 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>12 months</td>
<td>8 months</td>
</tr>
<tr>
<td>5 year survival</td>
<td>5-10%</td>
<td>0%</td>
</tr>
</tbody>
</table>
# Non small cell lung cancer

<table>
<thead>
<tr>
<th>Surgery</th>
<th>70% 5 year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1A (T1 N0 M0)</td>
<td>40% 5 year survival</td>
</tr>
<tr>
<td>Stage 1B (T2 N0 M0)</td>
<td>25% 5 year survival</td>
</tr>
<tr>
<td>Stage 2 (T1-2 N0 M0)</td>
<td></td>
</tr>
<tr>
<td>Surgery - with adjuvant chemotherapy (ie post surgery)</td>
<td>Absolute benefit of additional 4% at 5 years and disease free survival 5% at 5 years</td>
</tr>
<tr>
<td>CHART</td>
<td></td>
</tr>
<tr>
<td>Performance Status 0-1</td>
<td></td>
</tr>
<tr>
<td>FEV1 of 1.5 litres</td>
<td></td>
</tr>
<tr>
<td>(There are exceptions where the predicted values are low or damage to useful lung is thought to be low)</td>
<td></td>
</tr>
<tr>
<td>High Dose Palliative Radiotherapy</td>
<td></td>
</tr>
<tr>
<td>Improves median survival by 2 months</td>
<td></td>
</tr>
<tr>
<td>By 6% at 1 year</td>
<td></td>
</tr>
<tr>
<td>By 3% at 2 years</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy Stage 4</td>
<td></td>
</tr>
<tr>
<td>Performance status 0</td>
<td>Median survival 10 months</td>
</tr>
<tr>
<td>Performance status 1</td>
<td>Median survival 7 months</td>
</tr>
<tr>
<td>Performance status 2</td>
<td>Median survival 4 months</td>
</tr>
<tr>
<td>Overall without chemotherapy</td>
<td>5% at 1 year survival</td>
</tr>
<tr>
<td>Overall with chemotherapy</td>
<td>25% 1 year survival</td>
</tr>
<tr>
<td></td>
<td>(NB in those who are fit enough)</td>
</tr>
<tr>
<td></td>
<td>On average chemotherapy extends life expectancy by 2 months</td>
</tr>
</tbody>
</table>

50
Informing the Primary Care Team

- Following communication of the diagnosis of lung cancer to a patient then the primary care physician should also be informed of the diagnosis.

- The general practitioner should be informed of the diagnosis by the end of the following working day, preferably by fax.

- The general practitioner should be made aware of the information which has been given to the patient and, if possible, an outline of the planned treatment.

- If the diagnosis is made as an inpatient, the Primary Care Team should be informed on discharge from hospital if communication has not already taken place.

- Hospital nursing staff / Lung Cancer Nurse Specialist should liaise with the relevant community teams if required and agreed with the patient i.e. District Nurses, Occupational Therapists, Physiotherapists, Dieticians, Care Homes, Benefits Advisor, Social Services, Hospice, Palliative Care Team.

- Major alterations to the management plan should be communicated to the general practitioner.

- Similarly, if alterations are made by the general practitioner these should be communicated to the hospital. A patient held record, where available, would be a suitable means of such communication.
Specialist Nursing

- The NICE Clinical Guideline states “Ensure that a lung cancer clinical nurse specialist is available at all stages of care to support patients and carers”.

- The North of England Cancer Network supports the recommendation within the Cancer Reform Strategy that Commissioners should work with providers to ensure that patients experience good continuity of care and that particular consideration should be given in this respect to the role of the Clinical Nurse Specialist.

- The North of England Cancer Network recognises that lung cancer specialist nurses and thoracic surgical specialist nurses are a fundamental part of the lung cancer team and it is recommended that each Trust involved in the management of patients with lung cancer supports and properly funds the required number of nurses.

- The value of site specific nurses has been highlighted over a decade ago and the role of site specific nurses has been endorsed within national guidelines.

- The National Lung Cancer Audit 2010 found that of patients seen by a Lung CNS, 64.8% went on to receive treatment (2). Out of those patients who did not see a Lung CNS just 30.4% were given treatment (2).

- The NICE Clinical Guideline 121: The diagnosis and treatment of lung cancer (update) shows that the most common case load for a lung cancer nurse specialist is between 100-150 cases per year (1). It is thought that once a CNS has a bigger case load than this they are unlikely to be able to give patients the time they need to have a positive experience and to achieve the best possible outcomes.
• The National Lung Cancer Audit 2010 recommends that over 80% of lung cancer patients should be seen by a Lung CNS (2). Also it recommends 80% of patients should have a Lung CNS present when they receive a diagnosis (2). As a Northern Network we should aim to ensure patients have access to a Lung CNS at all times.

• Lung cancer nurses help to facilitate the effective provision of high quality patient centred care.

• It is recommended that the lung cancer nurse specialist should be made aware of all patients diagnosed with lung cancer.

• In particular, it is recommended that each unit should have one or more trained lung cancer nurse specialists to see patients before and after diagnosis, to provide continuing support, and to facilitate communication between the secondary care team, the GP, the community care team and the patient.

• It is recommended that within the network the lung cancer nurses meet regularly and form a mutually supportive group to develop the role.

• It is recommended that the lung cancer nurses provide:
  - Emotional and social support to patients and carers
  - Help with the provision of information
  - Facilitate communication with patients and carers
  - Facilitate communication within the health care teams
  - Co-ordinate services and investigations.

• It is recommended that local considerations are made with regard to the specific job plan arrangements of the lung cancer nurses. Different working arrangements are currently in place within different units, and within surgical centres, thoracic surgical nurse specialists should be employed.
- It is recommended that the nurses working together strive to determine the most appropriate model and work within each unit to deliver the highest standard of care. Models currently in place include hospital based nurses and nurses who work across both hospital and community.

- It is recommended that the lung cancer nurses work closely with the cancer pathway co-ordinator and cancer data managers in order to track patients.

Ref:
1. NICE, CG121: The diagnosis and management of lung cancer (update), April 2011
2. NHS Information Centre, National Lung Cancer Audit 2010, May 2011
Clinical Trials

The Cancer Reform Strategy states that “in order to ensure that we build for the future of cancer services there is a need for increased support for research.” This statement underpins the need for promoting research to fill the gaps in the evidence and spreading good practice.

The NECN Research Networks will work with the Service Network to promote integration of research into routine practice.

Both NECN Research Networks will be meeting the performance based working proposals for the National Cancer Research Network (NCRN). This includes maintaining overall accrual and improving accrual into randomised controlled studies, (RCT’s) with the aim being to provide as wide reaching a portfolio as possible across the NECN. There is a need to ensure that the Networks portfolios are inclusive of trials for all disease groups and that there is an expansion of pre-malignancy and non-cancer screening trials. Both Networks believe it is important that patients within the NECN have equity of access to trials open.

- New initiatives to strengthen research into prevention of cancer are underway. The Research Networks will work with key stake holders and the Primary Care Research Networks to ensure that patients in the North East and Cumbria have access to these trials.

- The CRS states that there is funding for screening trials and the Research Networks will support the setting up and coordination of screening trials.

- The NCRN has an important role in identifying potential new therapies and making sure that clinical trials are undertaken in a timely manner. NCRN engages with Industry and NICE with the aim of maximising the impact of NCRN trials on subsequent NHS Practice. There will be further investment over the next 10 years into researching cures and treatments of the future. The Research Networks will ensure they maintain a wide reaching balanced portfolio and promote industry trials.
Access to high quality information is a prerequisite for patients to be able to participate in decision making about their care and this includes research trials. All staff need to be aware of research portfolios so they can ensure they provide patients with relevant information.

Reducing inequalities in equity of access to cancer trials.

Promoting research proposals on cancer in equalities – encouraging more trials which include older people and ensuring that children and young adults are treated at centres where a complete portfolio of relevant trials is supported.

NCRI will help fund research on data collected by the National Cancer Intelligence network (NCIN), facilitating a more informed analysis of cancer services.

To ensure research is incorporated in World Class Commissioning for cancer.

To work more closely with our Patient and Carer Group, particularly in relation to equity of access for patients to clinical trials. We hope they will be able to help us provide a patients perspective and help support us raise awareness.

The Cancer Reform Strategy supports the need for promoting integration of research into routine practice and the NECN Research Networks are keen to advance this concept.

An agreed list of clinical trials for the Network can be found on the following website: www.necn.nhs.uk/research/portfolio-and-recruitment/

To review the current National Cancer research Network portfolio of Lung trials access the following website: http://public.ukcrn.org.uk/search/
Audit

Hospitals in the Northern of England Cancer Network area have agreed to participate in the National Lung Cancer Audit (LUCADA).

In addition to this, one Network agreed audit will be carried out. This will usually be agreed at the Lung NSSG. Audit is a requirement for Peer Review.

LUCADA data collection

The National Clinical Lung Cancer Audit (LUCADA, 2007) has been established for several years with annual reports. It is expected that all units submit data to LUCADA.

- It is recommended that each cancer unit establish a robust system for prospective LUCADA data collection in order to allow for clinical audit.

- It is recommended that each cancer unit is familiar with the LUCADA reports and generates appropriate action plans in line with the key recommendations identified from the reports.

- In particular each unit must strive to:
  - Submit data for 100% of cases.
  - Collect data for the key casemix variables stage, performance status and co-morbidity.
  - Note that histological and cytological confirmation rate is considered in the LUCADA report as a marker for quality of care, along with aspects of specialist nurse involvement.
  - Be aware of their own anti-cancer treatment rates in comparison with the national average.

Record Keeping

The responsibility for collecting the Cancer Registry Dataset will change from being a Registry responsibility to a Trust responsibility in the near future. It is
essential therefore to ensure that information required for Cancer Registry and Audit should be recorded clearly in all patients’ notes.

National Cancer Waiting Times Targets & Data Collection

- Patients referred by general practitioners with suspected lung cancer should be seen within two weeks of referral in a respiratory physician’s clinic.

- Inpatient referrals to a respiratory physician from other hospital consultants should be seen within two working days of receipt, and outpatient referrals within two weeks.

- National Cancer Waiting Times Targets require that no more than 31 days should elapse between the decision to treat and the start of treatment (of any modality).

- National Cancer Waiting Times Targets require that no more than 62 days should elapse between the date the GP decides to refer the patient and the commencement of treatment (of any modality).

- National Cancer Waiting Times Targets require that all subsequent treatments be carried out within 31 days of decision to treat. This will include treatments for all cancers including metastasis and recurrence (any modality).

- National Cancer Waiting Times Targets require that any patient that is deemed suitable to be upgraded to ‘two week rule’ status should wait no more than 62 days from receipt of referral to first treatment (any modality).

- Patients presenting in ways other than by direct GP referral to the MDT should have similarly rapid diagnosis and treatment, and should not be disadvantaged by “target patients.”
The Cancer Registry Dataset, information on National Cancer Targets and Network/National audits is available from Cancer Information Managers or Cancer Services Managers.
Treatment General Principles

- The management of lung cancer is complex and the treatment options available, offered and / or accepted by individual patients are often very different. It is therefore essential that all patients are carefully assessed and an individual treatment plan discussed with each patient.

- Information must be given sensitively and the information given suitable for each patient with the back up of written information appropriate to that individual. The guidelines described above should be followed in order to promote high quality clinical care.

- It is recommended that the patient is advised that their management is discussed at a multidisciplinary meeting and that it is not just one doctor who decides on the best course of action.

- It is recommended that the patient is advised that the multidisciplinary team is there in order to provide the patient with information and to assist in decision making, clearly describing options with associated risks and benefits.

- It is recommended that the patient understands that whatever decision is made by the patient, the multidisciplinary team will support that individual and that there is no pressure to accept any one type of treatment. Should the patient decide on no active treatment then they should be made aware that the team will continue to look after them.

- It is recommended that the patient should be able to see different members of the specialist team in order to make a decision regarding treatment. For example, the patient may see the respiratory physician, then an oncologist and a surgeon in order to make their final preferred treatment option.
**Smoking Cessation**

- Inform patients that smoking increases the risk of pulmonary complications after lung cancer surgery.
- Advise patients to stop smoking as soon as the diagnosis of lung cancer is suspected and tell them why this is important.
- Offer nicotine replacement therapy and other therapies to help patients stop smoking in line with smoking cessation services.
- Do not postpone surgery for lung cancer to allow patients to stop smoking.
- The management of lung cancer is described in more detail in terms of surgery, chemotherapy and radiotherapy for each of the following categories:
  - Non-Small Cell Lung Cancer
  - Small Cell lung cancer
  - Mesothelioma
  - Thymoma
Surgery

- When evaluating surgery as an option for patients with NSCLC, consider using a global risk score such as Thoracoscore to estimate risk of death. Ensure the patient is aware of the risk before giving consent for surgery.

- Suitable patients should be referred promptly for surgery, and cases in which there is doubt about operability should be discussed as soon as possible with a lung cancer surgeon. Performance status should be recorded in all patients.

- Patients may be clearly unsuitable for thoracotomy by virtue of poor performance status, obvious metastases, recurrent laryngeal nerve palsy, malignant effusion, paralysed hemi-diaphragm, other significant life threatening illness or unwillingness to undergo surgery.

- Investigations performed at the initial assessment may also indicate unsuitability for surgery. Prior to surgical referral all patients should have:
  - full blood count
  - urea and electrolytes
  - liver and bone chemistry
  - spirometry
  - ECG

Cardiovascular function

- Avoid surgery within 30 days of myocardial infarction
- If the ECG is abnormal, or there is a clear history of angina, then an exercise test should be arranged.
- Seek a cardiological review in patients with an active cardiac condition, or three or more risk factors, or poor cardiac functional capacity.
- Offer surgery without further investigations to patients with two or fewer risk factors and good cardiac functional capacity.
- Optimise any primary cardiac treatment and begin secondary prophylaxis for coronary disease as soon as possible.
• Continue anti-ischaemic treatment in the perioperative period, including aspirin, statins, and betablockers.
• If a patient has a coronary stent discuss perioperative anti-platelet treatment with a cardiologist.
• Consider revascularisation (percutaneous or CABG) before surgery with chronic stable angina and conventional indications for revascularisation.

**Lung Function**

• Perform spirometry in all patients being considered for treatment with curative intent. Measure TLCO if breathlessness is disproportionate or there is other lung pathology (for example fibrosis).
• Offer patients surgery if they have FEV1 within normal limits and good exercise tolerance.
• Offer patients with predicted postoperative FEV1 TLCO below the recommended limit of 30% the option of undergoing surgery if they accept the risks of dyspnoea and associated complications.
• When considering surgery perform a segment count to predict postoperative lung function.
• Consider using shuttle walk testing (using a distance walked of more than 400m as a cut off for good function) to assess fitness for patients with moderate to high risk of postoperative dyspnoea.
• Consider cardiopulmonary exercise testing to measure VO2 max and assess lung function in patients with moderate to high risk of postoperative dyspnoea, using more than 15ml/Kg/minute as a cut off for good function.

**General Considerations**

• If FBC and Urea & electrolytes are abnormal, there may be other explanations for this and the case should be discussed in the MDT. Other investigations may be necessary in some cases including:
• bone scan (if bone pain, or abnormal bone biochemistry).
• mediastinoscopy may be necessary except those with peripheral stage I/II tumours with no demonstrable hilar or mediastinal lymphadenopathy on
PET scan. Mediastinoscopy is strongly advised for central tumours even when the PET scan is negative in this area.

- Endobronchial ultrasound can be used where available, but should be followed by a mediastinoscopy in the setting of a negative result.
- Anterior mediastinotomy is the preferred invasive staging procedure in patients with left upper lobe tumours and enlargement of aortopulmonary window nodes.
- Pleural aspiration and biopsy (if effusion is present).
- Transfer factor and differential perfusion scan (if lung function is borderline): in general a post-operative predicted FEV₁ of 40% is required for surgery.
- All patients who are candidates for thoracotomy should have a staging CT scan and a separate PET scan and all patients undergoing radical surgery should have a CT head scan before surgery. The images should be available at the time of consultation with the thoracic surgeon. Performance status should be recorded in all patients. Patients with PET positive mediastinal nodes should have mediastinal staging with as needed a mediastinoscopy unless there is a chain of nodes and the primary tumour is known to be a NSCLC.
- Patients should be considered suitable for surgery if they are fit enough for operation and have a non-small cell tumour of stage I or II. Essentially this encompasses technically resectable primary tumours without spread beyond hilar lymph nodes and without distant metastases. Patients with evidence of metastases in the same lobe should be offered surgery.
- Patients with confirmed stage IIIA (N2) disease should not be offered surgery outwith a trial but surgery following chemotherapy can be considered in these patients. They should be discussed in an MDT. In general a pneumonectomy should be avoided in this class of patients and radiotherapy should be offered.
- Offer patients with NSCLC who are medically fit and suitable for treatment with curative intent lobectomy (either open or thoracoscopic) as the treatment of first choice. For patients with borderline fitness and smaller tumours (T1a-b, N0, M0) consider lung parenchymal sparing operations.
(segmentectomy or wedge resection) if a complete resection can be achieved.

- For all patients with stage I or II NSCLC undergoing surgical resection – usually a lobectomy or a pneumonectomy – clear surgical margins should be the aim. Offer more extensive surgery (bronchongioplastic surgery, bilobectomy, pneumonectomy) only when needed to obtain clear margins.

- Sleeve lobectomy offers an acceptable alternative to pneumonectomy for patients with stage I or II NSCLC who have an anatomically appropriate (central) tumour. This has the advantage of conserving functioning lung.

- For patients with T3 NSCLC with chest wall involvement who are undergoing surgery, complete resection of the tumour should be the aim by en bloc chest wall resection.

- All patients undergoing surgical resection for lung cancer should have systematic lymph node sampling to provide accurate pathological staging.

- Ensure that mechanisms are in place to support the entry of eligible patients into clinical trials, subject to the patient giving fully informed consent. The MDT should record the reasons for patients not being entered into trials that are open.

- Offer patients with stage I-III NSCLC who are not suitable for surgery an assessment by a clinical oncologist specialising in thoracic oncology for radiotherapy with curative intent.

- Consider surgery in patients with early stage Small cell lung cancer (T1-2a, N0, M0)
Non Surgical Management of Lung Cancer

Radiotherapy

Non-Small Cell Lung Cancer (NSCLC)

Radical Radiotherapy

- A clinical oncologist specialising in thoracic oncology should determine suitability for radiotherapy with curative intent taking into account performance status and co-morbidities.
- When surgery has been excluded as an option, curative non-surgical oncological modalities should be considered for patients with stages IA to IIIA non-small cell lung cancer (NSCLC) and for selected patients with stage IIIB NSCLC.
- Combining chemotherapy with radical radiotherapy has been shown to have survival advantages for patients with stage III disease. In addition, chemotherapy prior to radiotherapy may be considered in patients with bulky stage IB and II disease.
- Radical radiotherapy will be 3-D conformally planned and guided by dose-volume histograms for both tumour volume and normal tissue tolerances. The percentage of normal lung receiving more than 20 Gy should not exceed 30% (V20 < 30%).
- CHART may be offered to patients considered for radical RT either as single modality treatment or after induction chemotherapy in a trial setting.
- Pre-treatment FEV-1 should be > 1.0 litre; kCO should be > 50% of predicted.
- All patients undergoing radical oncology treatment with curative intent should have a CT head scan before treatment commences.
- Wherever possible, patients should be considered for entry into clinical trials.
- Patients receiving radiotherapy with curative intent should be part of a national quality assurance programme.
Continuous Hyperfractionated Accelerated Radiotherapy (CHART)

This has been proven to provide an enduring survival advantage for patients with NSCLC when compared to the conventional dose of 60Gy in 30 fractions\(^2\). CHART involves the administration of 54Gy in 36 doses of 1.5Gy each, delivered 3 times daily over a total of 12 days.

CHART has not been compared to 55Gy in 20 fractions in any clinical trials. In terms of BED in 2 Gy fractions, 55Gy in 20 fractions is equivalent to 66 Gy in 33 fractions. For this reason, 55Gy in 20 fractions is a very reasonable alternative to CHART and is widely used in the UK.

Conventional Radical Radiotherapy

This involves the administration of 55Gy in 20 fractions over 28 days. Where a cancer is peripherally situated, 55Gy in 15 fractions delivered over 21 days or 60Gy in 20 fractions delivered over 28 days may be chosen.

Stereotactic Body Radiotherapy (SBRT)

In the USA and Europe, this is fast becoming the standard of care for management of medically inoperable stage I and IIA disease situated in the lung periphery. The NECN now has the technology to deliver SBRT.

Post-Operative Radiotherapy

The routine use of adjuvant postoperative radiotherapy may confer a survival disadvantage\(^4\). However, in some situations, post-operative radiotherapy may reduce the risk of locoregional recurrence (e.g. following resection of N2 disease or, in those patients with macroscopic or microscopic residual disease). CHART or conventional RT doses as above should be considered.
Palliative Radiotherapy

- Palliative thoracic radiotherapy should be reserved for patients with metastatic disease or locally advanced disease not amenable to radical treatment. In general, short courses offer as good palliation as fractionated ones and are recommended for poor prognosis patients with chest symptoms. Selected patients with good performance status and no obvious evidence of metastases should be considered for higher dose regimens\(^1\,\^3\).

Technique (see Departmental Protocols for details)

- Treat as a parallel opposed pair. Dose regimens:
  - 10Gy mid-plane dose (MPD) in a single fraction for patients with metastatic disease or WHO PS 2-4 and maximum field size <200 cm\(^2\)
  - 20 Gy MPD in 4/5 fractions over 1 week where volume >200 cm\(^2\), or where mediastinal obstruction exists (stridor or extrinsic oesophageal compression) OR 17 Gy in 2 fractions, one week apart.
  - 36 Gy MPD in 12 fractions over 2½ weeks without spinal cord shielding for patients with PS 0-1, in whom all macroscopic disease can be encompassed within radiotherapy portals. 39 Gy in 13 fractions over 2½ weeks is an alternative, but spinal shielding is required.

- Length of cord should not normally exceed 14 cm.

- Regimens may be repeated (off cord) especially if there has been a good response to initial treatment and there is a reasonable period between treatments.

- Patients with major airways obstruction may require urgent radiotherapy.

- Palliative single fractions or short courses of radiotherapy may be prescribed to sites of distant metastatic disease (e.g. for bone pain, intracranial disease, spinal cord compression).
Small Cell Lung Cancer (SCLC)

There is increasing data supporting the earlier use of RT in SCLC. Recent North American studies have suggested that patients with good performance status and limited disease may gain improved disease free survival and overall survival if concurrent chemo-radiotherapy is employed as the induction therapy\(^5\). Patients with limited stage disease, normal biochemical and haematological parameters, of good performance status (WHO PS 0-1) and with sufficient respiratory reserve should be offered concurrent chemo-radiotherapy.

Otherwise patients with limited stage disease who attain a complete response with induction chemotherapy should then be offered consolidation thoracic irradiation and prophylactic cranial irradiation.

Thoracic irradiation (TI) in SCLC

- Concurrent chemo radiation is administered following the RTOG study protocol. This uses Cisplatin and Etoposide plus 3-D conformally planned radiotherapy to a dose of 45 Gy in 25 fractions over 30 days. Where the V20 is less than 25%, 50Gy in 20 fractions may be used.

- Sequential consolidative thoracic irradiation is recommended for those patients with WHO performance status 0-2, with limited stage disease and who have achieved a complete response following induction chemotherapy. This is again 3-D conformally planned to a dose of 50-55Gy in 20-25 fractions over 30 days.

- Patients who have achieved less than a complete response following chemotherapy may be offered thoracic irradiation as an additional modality of treatment for symptomatic intra-thoracic disease (doses as for palliative treatment of NSCLC).
Palliative thoracic irradiation may also be offered to patients who, for any reason have not received chemotherapy. These patients are frequently of poor performance status and require palliation of intra-thoracic disease.

**Prophylactic Cranial Irradiation (PCI) in SCLC**

- It is recommended that patients with small cell lung cancer in good prognosis categories who have achieved a complete response to chemotherapy receive whole brain irradiation at a dose of 30 Gy in 10-15 fractions over 2-3 weeks.

- PCI is also recommended for patients with extensive stage SCLC who have had a response to chemotherapy and have a PS of 0-2. A dose of 20 Gy in 5 fractions is the most commonly used schedule.

- PCI is delivered using parallel opposed, lateral fields. The field can be set up in the clinic. Use the surface anatomy for the base of skull as the inferior edge of the field (supra-orbital ridge to tragus of ear).

**Toxicity of Treatment**

**Chest**

- Acute side effects of thoracic irradiation may include fatigue, chest pain (usually with high doses per fraction), nausea, oesophagitis, altered taste, pneumonitis and skin reactions.\(^6\)

- On the whole thoracic irradiation is relatively well tolerated although patients who have had previous chemotherapy may experience more pronounced acute side effects.

- Late side effects are inevitable if the patient lives long enough to experience them. They can be kept to a minimum by careful planning where appropriate, but may include fibrosis (lung, oesophagus, chest wall) or pericarditis.
Brain

- Acutely, patients may experience headache, nausea & vomiting, somnolence and alopecia. The long-term side effects of cranial irradiation at the doses employed for PCI are few. Reports of neuropsychological sequelae have generally been in patients receiving chemotherapy at the same time as radiotherapy, and recent studies\(^7\)\(^8\) have shown no significant difference in neurocognitive tests between a group of patients undergoing PCI in addition to chemotherapy and a group receiving chemotherapy alone.

- Prophylactic steroids may relieve the acute symptoms of cranial irradiation.

Endobronchial brachytherapy

Endobronchial brachytherapy may have a limited role in the retreatment of patients with symptoms due to endobronchial tumour or external compression of a bronchus by tumour. Suggested dose: 10-15 Gy at 1cm radius.

Trials

Where possible, important clinical questions should be addressed in the context of clinical trials. These areas of interest include the role of concurrent chemoradiotherapy in both NSCLC and SLCLC, the optimal fractionation regimen for thoracic and cranial irradiation for SCLC and the best regimen to achieve optimal palliation in patients of both good and poor prognosis status. Recommendations for approved studies should be made through the Network Site Specific groups and MDTs in collaboration with the National Cancer Research Network team.

Ensure that mechanisms are in place to support the entry of eligible patients into clinical trials, subject to the patient giving fully informed consent. The MDT should record the reasons for patients not being entered in to trials that are open.
Chemotherapy

General Principles

- Consideration should be given in the first instance as to whether or not chemotherapy is appropriate for the individual. This decision will be based on the extent and type of disease as well as performance status and will take into account the individual wishes of the patient.

- The aim of the chemotherapy (curative, neoadjuvant, adjuvant or palliative) should be defined prior to administration and this should be discussed with the patient together with the potential side effects of the treatment.

- Chemotherapy should be administered in accordance with the published recommendations of the JCCO using whenever possible protocols which have been agreed by the NECN lung group. Because chemotherapy is likely to cause significant toxicity in terms of bone marrow suppression, alopecia, nausea and vomiting and fatigue it should only be administered by teams which include Oncology Specialists, with the appropriate skills and training.

- The patient should be closely monitored while on treatment and every effort made to address quality of life issues.

- For patients receiving palliative or neoadjuvant chemotherapy, treatment should be discontinued if there is no evidence of a response after 2 cycles or after 1 cycle if there is evidence of progressive disease. Chemotherapy should also be discontinued if the patient has unacceptable toxicity even in the absence of progressive disease.

- Ensure that mechanisms are in place to support the entry of eligible patients into clinical trials, subject to the patient giving fully informed consent. The MDT should record the reasons for patients not being entered into trials that are open.
Small Cell Lung Cancer (SCLC)

Staging

- Staging using the limited/extensive disease categories as per the NICE guidelines is of prognostic value in patients with small cell lung cancer. Staging alone however should not be the only guide to the intensity of therapy as long term survival can occur in extensive stage patients. The patient assessment should include history and examination, performance status, CXR, FBC, Serum Biochemistry including LFT’s & LDH and CT of chest, upper abdomen and head.

- The good prognosis group consists of patients with good performance status (WHO 0,1, Karnofsky greater than 70%) and not more than 1 of the following factors:
  - Extensive disease
  - Low serum sodium
  - Raised alkaline phosphatase
  - Raised AST
  - Raised LDH

Chemotherapy

- Arrange for patients with SCLC to have an assessment by a thoracic oncologist within 1 week of deciding to recommend treatment.

- Combination chemotherapy has been shown to increase survival and quality of life in patients with SCLC and is superior to single agent therapy even in poor prognosis patients.

Good Prognosis Patients

- The prognostic group studies have consistently shown that only the ‘good’ prognosis patients achieve long term survival.

- The recommended treatment in good prognosis patients with limited stage disease, normal haematological and biochemical parameters, good performance status and
sufficient respiratory reserve is concurrent chemoradiation with Cisplatin and Etoposide (see chemotherapy protocols for details).

- All other good prognosis patients should be offered a combination of Carboplatin or Cisplatin and Etoposide (see chemotherapy protocols for details). Response should be assessed after 2 cycles and only continued if the tumour is responding. Dose modification may be required in the presence of unacceptable toxicity (See network protocols for guidance). A total of 4-6 cycles should be given unless there is evidence of progressive disease or unacceptable toxicity.

- Good performance stage (PS 0,1,2) patients with limited stage disease who have not undergone concurrent chemoradiation but who achieve a complete response or good partial response should be offered consolidative thoracic radiotherapy on completion of their chemotherapy.

- Patients who achieve less than a complete response may be referred for consideration of palliative radiotherapy if symptomatic.

- Good prognosis patients (limited and extensive disease) who achieve a partial or complete response to chemotherapy should be referred prior to their penultimate cycle of treatment for consideration of prophylactic cranial irradiation (PCI).

**Poor Prognosis Patients**

- Patients should be treated with palliative intent using a combination of Carboplatin & Etoposide as per the good prognosis patients or a combination of Vincristine, Doxorubicin and Cyclophosphamide (see chemotherapy guidelines) in patients not suitable for platinum based chemotherapy. Response should be assessed after 2 cycles and chemotherapy only continued if the patient is responding and toxicity is acceptable. Responding, patients should receive between 4 – 6 cycles of treatment. The patient should be re-discussed at the multidisciplinary meeting regarding a referral for radiotherapy following completion of chemotherapy in the presence of symptomatic disease.
Clinical trials

- Ensure that mechanisms are in place to support the entry of eligible patients into clinical trials, subject to the patient giving fully informed consent. The MDT should record the reasons for patients not being entered in to trials that are open.

Disease Relapse

- In patients who relapse more than 3 months following completion of chemotherapy consideration should be given to retreating with their original chemotherapy regime, eg oral Topotecan, providing this is in accordance with patient wishes and their performance status is acceptable. Entry into ongoing clinical trials may be considered if the patient is agreeable. Palliative radiotherapy or symptomatic care however may be in the best interests of the patient.

- If relapse is less than 3 months following treatment these patients fall into a particularly poor category. These patients may be considered for treatment with an alternative chemotherapy regime, for example, oral Topotecan though response rates are likely to be low, or entry into an appropriate clinical trial. Again, palliative radiotherapy or symptomatic care may be more appropriate than further chemotherapy.
Non-Small Cell Carcinoma

Neoadjuvant Chemotherapy

- Neoadjuvant chemotherapy is not routinely recommended in patients with surgically resectable disease, but downstaging neoadjuvant chemotherapy may be considered in patients whose initial staging precludes them from surgery or radical radiotherapy. This must be discussed at the thoracic MDT.

Adjuvant Chemotherapy

- The meta-analysis of 1995 has shown an absolute survival benefit for adjuvant therapy of 5% for Cisplatin based regimes, but the 95% confidence intervals are wide making the actual benefit difficult to assess. Subsequent studies have confirmed a benefit for adjuvant chemotherapy in selected groups of patients. Adjuvant chemotherapy is therefore recommended in patients with stage T1-3, N1-2 M0 NSCLC and T2-3 N0 M0 NSCLC with tumours greater than 4cm in diameter who are of good performance status 0-1, preferably within 8 weeks of surgery. The proposed regimes are Carboplatin and Paclitaxel or Cisplatin and Vinorelbine (see chemotherapy protocols for details).

Combined Chemoradiation

- Consider chemoradiotherapy for patients with stage II or III NSCLC who are not suitable for surgery. Balance potential benefit in survival with the risk of additional toxicities.

- Combining chemotherapy and radiotherapy for patients with stage III disease has been shown to have survival benefits. All patients with good performance status who have stage IIIA disease who are not suitable for surgery and selected IIIB NSCLC patients should be offered combined chemoradiation treatment. Where the patient’s PS, renal function and PFTs allow, concurrent chemoradiation using the SOCCAR regimen should be considered as standard.
• Ensure all patients potentially suitable for multimodality treatment (surgery, radiotherapy and chemotherapy in any combination) are assessed by a thoracic oncologist and a thoracic surgeon.

Palliative chemotherapy

• In patients with stage 3B (not suitable for radical treatment) & 4 disease, chemotherapy may have a role both in symptomatic benefit and possible prolongation of survival. Patients who fit into this category should be fit (PS 0, 1, 2) and be agreeable to treatment. The recommended protocols are a combination of a platinum drug (Cisplatin or Carboplatin) and Pemetrexed for patients with non-squamous histology and for those with squamous cell cancer or non small cell lung cancer not otherwise specified and a 3rd generation drug (Vinorelbine, Gemcitabine, Paclitaxel or Docetaxel) (usually 4 cycles) with single agent Vinorelbine or Gemcitabine reserved for those not suitable for platinum based regimes (see chemotherapy protocols for details). Note patients with non-squamous histology should now be offered Pemetrexed and a Platinum drug.

• In patients with Stage 3B disease who have had a response to chemotherapy it may be appropriate to re-discuss the patient at the multidisciplinary meeting regarding referral for thoracic radiotherapy. Patients with stage 4 disease should be re-discussed at the multidisciplinary meeting regarding a referral for radiotherapy in the presence of persisting symptomatic disease.

• All patients within this group should be considered for entry into appropriate clinical trials. Current trials include the following:
  ▪ FRAGMATIC

• In patients not suitable for chemotherapy, consideration should be given as to whether they may be suitable for the TOPICAL study, which is looking at the role of Tarceva, an EGFR inhibitor, in the management of patients with advanced NSCLC.

Tyrosine Kinase Inhibitors

(NICE Technology Appraisal Guidance 192, 2010)
• This guidance states that Gefitinib is recommended as a treatment option for the first line treatment of people with locally advanced or metastatic non-small cell lung cancer (NSCLC) if
  1. They test positive for epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation and
  2. The manufacturer provides gefitinib at the fixed price agreed under the patient access scheme. Gefitinib is given as an oral 250mg tablet daily, and is being supplied by the manufacturer at a fixed price under a patient access scheme. Under this scheme there is a fixed cost of £12200 per patient once the third pack is provided, so assessment of response to treatment before the end of the 2nd month is essential.”

• The NECN Lung NSSG recommends that this guidance is followed. Current policy which is regularly reviewed (July 2011) is to request EGFR mutation testing on all suitable patients following MDT discussion. In addition EGFR mutation testing can be requested before MDT discussion at the discretion of the treating clinicians if it is highly likely that this treatment might be a possibility. EGFR mutation testing can also be requested at any later stage if the clinicians feel that this would be clinically beneficial to the patient. Second Line Chemotherapy and TKIs

• In good performance status patients who have had a durable response (more than 6 months) to first line chemotherapy it may be appropriate to consider retreatment with the original regime. The alternative recommendation is consideration of single agent Docetaxel as per the NICE guidelines. Again all patients should be considered for entry into appropriate clinical trials.

• Patients may be offered erlotinib (Tarceva) as an alternative to docetaxel. This decision will be at the discretion of the oncologist and will take into account patient preference. In patients with BAC, erlotinib should be considered the drug of choice.

Managing Endobronchial Obstruction

• When patients have large airway involvement, monitor (clinically and radiologically) for endobronchial obstruction to ensure treatment is offered early.
• Offer external bean radiotherapy and or endobronchial debulking or stenting for patients with impending endobronchial obstruction.
• Every cancer Network should ensure that patients have rapid access to a team capable of providing interventional endobronchial treatments.
• In the NECN this is provided at Freeman Hospital for all procedures with provision for some procedures at James Cook University Hospital.

Follow up and Patient Perspectives
• Offer all patients an initial specialist follow up appointment within 6 weeks of completing treatment to discuss ongoing care. Offer regular appointments thereafter, rather than relying on patients requesting appointments when they experience symptoms.
• Offer protocol driven follow up led by a lung cancer clinical nurse specialist as an option for patients with a life expectancy of more than 3 months.
• Ensure that patients know how to contact the lung cancer clinical nurse specialist involved in their care between their scheduled hospital visits.
• The opinions and experiences of lung cancer patients and carers should be collated and used to improve the delivery of lung cancer services. Patients should receive feedback on any action taken as a result of such surveys.
Malignant Mesothelioma

These Network guidelines on malignant mesothelioma are based on the British Thoracic Society statement on malignant mesothelioma in the United Kingdom, 2007, and the NICE guidelines for the use of Pemetrexed for malignant mesothelioma.

Epidemiology

- There has been a steady increase in the incidence of mesothelioma since cases were first recorded in the late 1960’s and it is estimated that the peak of the number of cases of mesothelioma will be reached sometime between 2011 and 2015 with mesothelioma accounting for approximately 0.7% of all deaths.
- There is widespread variation in the incidence of mesothelioma however the North East should be regarded as an area with high incidence.
- Asbestos fibres are regarded as the most significant risk factor for mesothelioma. Exposure to asbestos is usually directly attributable to occupational exposure although para-occupational exposures and non-industrial environmental exposures are also recognised. Mesothelioma can also be secondary to non-asbestos fibres such as Erionite identified in different areas of Turkey.
- The latency between first exposure to asbestos and mesothelioma is typically long with a median latency of 32 years, with a few cases occurring before 20 years but up to a third of cases occurring over 40 years from exposure. Recent studies suggest a possible mean latency of 41 years with a range of 15-67 years.
- There is currently the suggestion that cases of mesothelioma from specific high risk industries such as shipbuilding, railway engineering and asbestos manufacturing and construction are levelling off and possibly falling, whereas cases following exposure from a wider range of occupations are increasing. Currently workers with the highest risks are likely to be those with incidental exposures from those who have worked in building maintenance or similar occupations e.g. joiners.
• The risk of mesothelioma varies considerably in relation to the type of asbestos with the highest risks associated with amphibole asbestos with the lowest risk from chrisotile asbestos. This latter type was by far the most widely used type of asbestos in the UK, however evidence does suggest that historical exposures are likely to have involved a mixture of both types of fibres.

Clinical Features

• Typical presentation involves chest pain and dyspnoea often directly due to the disease. Symptoms can also occur secondary to the development of a pleural effusion with for example cough. Systemic features are often seen with weight loss and sometimes sweating.
• Malignant mesothelioma should be considered in any patient with either pleural fluid or pleural thickening especially if associated with chest pain.
• Malignant mesothelioma may present with persistent unexplained chest pain and a normal chest x-ray.
• Symptomatic metastatic disease from malignant mesothelioma is generally unusual at presentation.

Prognosis

• Prognosis is affected by a number of factors with worse prognosis associated with sarcomatoid histology and possibly male gender, advanced stage disease, poor performance status, leukocytosis and thrombocytosis.
• For malignant mesothelioma the median survival time varies from between eight and fourteen months and the disease is generally progressive with an overall poor five year survival although very occasionally patients can survive for a longer period.
• Epitheliod tumours have a better prognosis than other cell types.
Diagnosis

- The diagnosis is often difficult to achieve and is usually made through a combination of history, examination, radiology and pathology and on occasions despite all of the above diagnosis may remain difficult to make.
- The history of asbestos exposure is very important and a detailed occupational history is essential.
- Any patient in whom mesothelioma is expected should be promptly referred to a respiratory physician for further assessment.
- Pathological confirmation of the diagnosis is recommended unless the patient is frail or has advanced disease.
- A negative pleural biopsy and negative cytological results do not exclude mesothelioma and should lead to further investigation and/or follow up.
- CT scanning plays an important role in the diagnosis of mesothelioma.
- When a chest x-ray shows features suggestive of mesothelioma then a pleural tap and CT scan are reasonable initial investigations but very often need to be combined with a biopsy. With appropriate cytology a clinical and radiological diagnosis of mesothelioma is reasonable however if there is doubt, a biopsy is recommended.
- Biopsies can be obtained either from closed pleural biopsies, CT guided biopsies, medical thoracoscopic biopsies or surgical thoracoscopic biopsies. It is generally recognised that closed biopsies are less effective at reaching a diagnosis than a directed CT guided biopsy or thoracoscopic biopsy.
- Thoracoscopic biopsies also facilitate the drainage of fluid and immediate talc pleurodesis, particularly where the thoracoscopic appearances are clearly malignant.
- At times it may be difficult to confirm a diagnosis and a diagnosis may only emerge with time after repeat CT scans and/or biopsies. In general most equivocal cases eventually do turn out to be mesothelioma, with a persistent effusion unusual in the presence of benign pleural thickening.
Diagnostic Imaging

- Where a chest radiograph is suggestive of malignant pleural disease it is recommended that a copy of the report is sent to a designated member of the lung multi-disciplinary team, usually the chest physician.
- The multi-disciplinary team should have a mechanism to follow up such faxed reports.
- In patients with suspected malignant pleural disease a chest CT scan should be performed before pleural biopsy and/or thoracoscopy.
- CT scanning cannot reliably differentiated malignant mesothelioma from other causes of malignant pleural disease.
- Ultrasound guided pleural aspiration should be used as a safe accurate method of obtaining fluid if there is a small or loculated effusion.
- MRI scanning has a limited role in patients with malignant mesothelioma beyond CT scan.
- PET scanning may be useful in differentiating benign from malignant disease but this is not clear cut and PET scans done for pleural disease should be interpreted with caution.
- Radiological staging of patients with malignant mesothelioma should occur before radical surgery and/or clinical trial entry.
- CT scan features that in the past have been used to distinguish malignant from benign pleural disease include circumferential pleural thickening, nodular pleural thickening, parietal pleural thickening >1 cm and mediastinal pleural involvement. Whilst a positive predictive value of these features is high their absence does not exclude a diagnosis of pleural malignancy and CT scanning cannot reliably differentiate malignant mesothelioma from other malignancies.
- Some of the commonest features of malignant mesothelioma include circumferential nodular lung encasement, pleural thickening with irregular pleuro-pulmonary margins and pleural thickening with super-imposed nodules. Such features are often important for those patients with a poor performance status where a clinical diagnosis is made.
Pathology

- Pathological diagnosis may be obtained through cytology and/or histology.
- Establishing the nature of mesothelial proliferation in samples is regarded as a challenging aspect of diagnosis.
- The cellular origin of malignant mesothelioma is not clear, however it is suggested that tumours might arise from mesothelial cells that have the ability to differentiate along diverse lines.
- Various histopathological sub-types have been described. Despite this wide variation, it is generally regarded that tumours should be classified into one of three main types: epitheliod, sarcomatoid (with desmoplastic mesothelioma being a particularly aggressive form of the latter), and biphasic. Pathologists should attempt to specify the histological type of mesothelioma.
- Immunohistochemistry may be used in differentiating mesothelioma from other tumours. Careful consideration of the diagnosis should be made at the multi-disciplinary team meeting with active pathology involvement and if necessary further referral for an additional pathology opinion including referral of cases to recognised national experts if appropriate.
- It should be noted that there are some other rarer specific types of mesothelial tumour including well-differentiated papillary mesothelioma, multi-cystic mesothelial proliferation and solitary fibrous tumour.
- Pathologists should be prepared to submit samples for expert opinion in cases of diagnostic difficulties.
- The pathological diagnosis of diffuse malignant mesothelioma is not always straight-forward and interpretation should always be taken in context with fully knowledge of the clinical history, examination findings and radiological appearance.
General Management

- All patients with mesothelioma should be managed by a cancer and mesothelioma multi-disciplinary team and be under the care of a specialist (usually a respiratory physician).
- Ongoing follow up by a member of the multi-disciplinary team is usually regarded as appropriate.
- All patients should be discussed at a multi-disciplinary team meeting.
- Where there is diagnostic uncertainty, or where radical treatment is considered, cases should be referred to a specialist multi-disciplinary team.
- Written information about the disease and its medicolegal aspects should be made available to the patient and family.
- It should be remembered by all involved that all deaths have to be reported to the coroner.

Treatment Strategy

Management is orientated towards the following:

- Suitability for radical surgery and/or clinical trial entry
- Management of the pleural effusion
- Prophylactic radiotherapy to intervention sites
- Chemotherapy
- Compensation issues
- Supportive care requirements

Due to the nature of mesothelioma and its rarity in certain areas, it is recommended that patients should have access to a specialist multi-disciplinary team when necessary. There is no one number of occasions which defines a specialist multi-disciplinary team however it is more defined by an expressed interest and evidence of special interest in the diagnosis and management. It is however regarded that teams diagnosing fewer than ten to fifteen cases per year are unlikely to develop and retain the required
attributes. A typical specialist multi-disciplinary team meeting would be expected to discuss a minimum of 25 cases per year.

**Surgery**

- The role of surgical resection in malignant mesothelioma is very uncertain. Two approaches can be taken.
  1. A radical approach extra-pleural pneumonectomy.
  2. A less radical approach debulking surgery.
- Consideration of surgery for malignant mesothelioma should be made with considerable care and if necessary the patient should be referred to a specialist surgeon in this area.
- There are no randomised control trials to establish the role of surgery.
- Radical surgery should only be considered within a randomised trial.
- Surgery should be concentrated in centres where there is experience in performing extra-pleural pneumonectomies.
- The present claims for benefit are for surgery within multi-modality therapy.
- Patients should be aware of the potential of tri-modality treatment and given realistic information about all outcomes.
- It should be remembered that the nature, extent, pattern of growth and proximity of major organs makes mesothelioma impossible to eradicate completely without complete resection of the parietal and visceral pleura, the underlying lung, the diaphragm and the pericardium and that even following all of this surgery there are often doubts about resection margins.
- Operative mortality for extra-pleural pneumonectomy is between 4-9% with up to 60% of patients having significant complications.

**Management of Pleural Effusion**

- One of the central aims of mesothelioma management is early and successful pleurodesis improving symptom control and reducing the likelihood of a trapped lung.
• Due to the low diagnostic yield of closed procedures thoracoscopy is an extremely useful early technique both for diagnosis and management of pleural effusions.
• If a patient is unable to undergo thoracoscopy, medical talc/pleurodesis via an intercostal drain is an option. The dose of talc in this case should not exceed 4 grams.
• Some patients may suffer a trapped lung either at presentation or subsequent in the course of disease and in these circumstances rapid reaccumulation of pleural fluid can occur without the possibility for pleurodesis in which case indwelling pleural catheters may be inserted which can significantly improve the quality of life.

Radiotherapy
• Palliative radiotherapy provides pain relief in about half of patients.
• Palpable masses respond to radiotherapy in about half of all patients.
• Breathlessness and superior vena caval obstruction rarely respond to radiotherapy.
• Prophylactic radiotherapy may be due to chest wall implantation following invasive procedures. It is most applicable for patients with a better prognosis and after more invasive procedures. Prophylactic radiotherapy has been shown to reduce the risk of seeding of malignant cells reducing local recurrence at sites of previous intervention.

Chemotherapy
• Several chemo therapeutic agents can reduce tumour bulk and help symptoms.
• The combination of Pemetrexed and Cisplatin significantly prolong survival compared with Cisplatin alone.
• All patients with mesothelioma who have performance status 0-1 at diagnosis, have advanced disease and for whom surgical resection is
inappropriate should be offered treatment with Pemetrexed and platinum based chemotherapy (carboplatin or cisplatin).

**Supportive and Palliative Care**

- Support and palliative care for patients with mesothelioma and their families is very important.
- Supportive care includes: information giving, self-help and support, user involvement, symptomatic control, psychological support, social support, spiritual support, rehabilitation, complementary therapy, palliative care and end of life bereavement care.
- Most patients with malignant mesothelioma need symptom palliation from time of diagnosis onwards.
- Symptomatic and palliative care aims to provide relief from pain and other physical symptoms and to respond to emotional, psychology, social and spiritual needs.
- Clinical nurse specialists have an essential role in providing and co-ordinating care of patients and their carers. Lung cancer clinical nurse specialists act as a key worker facilitating the pathway of care for the patient and family throughout the illness. Patients with malignant mesothelioma and their carers should have access to a lung cancer clinical nurse specialist.
- The clinical nurse specialist should provide help and guidance to patients and their carers concerning entitlement to benefits and allowances.
- Physical, psychological, social and spiritual assessment may need to be repeated at several key times during the illness.
- Patient preference is particularly relevant when making treatment decisions about malignant mesothelioma.
- Timely access to the health care team is vital.
- Early involvement of a pain relief specialist is indicated if pain is not controlled after initial measures.
- Dyspnoea, cough and other symptoms should be managed according to palliative care guidelines.
Peritoneal Mesothelioma

- Peritoneal mesothelioma is related to asbestos exposure but is less common than pleural mesothelioma. The outlook is generally poor and no treatment has been shown to alter prognosis.

Benefits and Compensation for Mesothelioma

- Patients may be entitled to claim compensation in two ways:
  1. Claim for Industrial Injuries Disablement Benefit from the Department of Social Security or through the War Pension Scheme. Other benefits for incapacity and disability may also be payable.
  2. Common law claim for damages from the firm/firms where exposure to asbestos occurred.
- Industrial injuries benefit is awarded if the person is suffering from a prescribed disease or personal injury which developed after 4th July 1948. The claimant must be an employee and they should have worked in a scheduled occupation where they had been exposed to asbestos. A claim is pursued by contacting the local job centre plus/or the Department for Work and Pensions and obtaining the relevant form.
- Providing the claimant qualifies the individual should obtain 100% disability and have it backdated to the date of diagnosis.
- Mesothelioma caused by exposure to asbestos during service in the defence forces is compensated under the War Pension Scheme.
- In addition to the above Industrial Injuries Benefit and War Pension Scheme patients may obtain additional benefits. Additional benefits may include income replacement such as statutory sick pay or occupational sick pay and incapacity benefit. In addition help with excess cost of disability can come from attendance allowance and disability living allowance.
- Benefit schemes often change and the above may not be complete or have changed and it is recommended that where there is any doubt,
the specialist lung cancer nurse should seek the advice of a benefit specialist to ensure that the individual receives the most appropriate benefits.

- In addition to the above, patients can also consider seeking common law compensation. Clinicians seeing any patients with asbestos related lung disease should promptly advise the patients to consider seeking legal advice to reduce the risk of subsequent claims from mesothelioma being statute barred.
- For patients in whom neither an employer nor insurer can be identified a claim can still be made to the Department of Work and Pension under the Pneumoconiosis Act 1979.

**Mesothelioma References**

These Network guidelines have been broadly based on the British Thoracic Society Statement on Malignant Mesothelioma in the UK and also the NICE Guidelines for the use of Pemetrexed for Malignant Mesothelioma.

Thymic Tumours

Introduction

Thymic tumours are uncommon (incidence 0.15/100 000) and are broadly classified into thymomas and thymic carcinomas. Thymic tumours are the most common tumours of the anterior mediastinum, accounting for 20% of mediastinal tumours and 50% of all anterior mediastinal tumours. Over 90% of all thymic tumours occur in the anterior mediastinum, the remainder occurring in the neck or other mediastinal areas. Thymic carcinomas are much rarer comprising 1% of thymic malignancies. Thymomas are epithelial tumours generally considered to have an indolent growth pattern but malignant nonetheless because of potential for local invasion, pleural dissemination, and even systemic metastases. Most patients are between the ages of 40 and 60 years at the time of diagnosis with an equal gender distribution.

Thymomas often present incidentally, but may also present with pressure related symptoms such as chest pain and dyspnoea, or with associated paraneoplastic syndromes (most commonly myasthenia gravis (approx 30%)).

Overall prognosis for lower grade thymomas is excellent with cure rates in excess of 95%. Higher grade thymomas and thymic carcinomas have a poorer outlook. The 5 year survival for thymic carcinomas is 20-30%.

The differential diagnosis of anterior mediastinal masses

Lymphoma
Carcinoid
Germ Cell tumour
Thyroid tumours
Parathyroid tumours
Thymic cysts
Lymphangioma
Aortic Aneurysm
Histological Classification

Thymic tumours are classified histologically according to the WHO system, which is important for management and prognosis:

<table>
<thead>
<tr>
<th>WHO classification of thymomas</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WHO type</strong></td>
</tr>
<tr>
<td>Type A</td>
</tr>
<tr>
<td>Type AB</td>
</tr>
<tr>
<td>Type B1</td>
</tr>
<tr>
<td>Type B2</td>
</tr>
<tr>
<td>Type B3</td>
</tr>
<tr>
<td>Type C</td>
</tr>
</tbody>
</table>

From Nakagawa et al

Staging

The modified Masaoka staging system is useful for management and prognosis. This anatomical classification assesses the degree of invasiveness of the tumour, including macro- and microscopic invasion of the capsule and surrounding structures.

<table>
<thead>
<tr>
<th>Modified Masaoka staging system</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
</tr>
<tr>
<td>II.</td>
</tr>
</tbody>
</table>

From Okumura et al
III  
A) Macroscopic invasion into neighboring organs i.e pericardium, great vessels, lung  
B) With invasion of great vessels

IV  
A) Pleural or pericardial dissemination  
B) Lymphogenous or haematogenous metastasis

From Masaoka et al, Eur J Cardiothoracic Surg 1994; 251-3

Influence of Masaoka stage on complete resection, recurrence and survival  
(n = 1320)

<table>
<thead>
<tr>
<th>Masaoka stage</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IVA</th>
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</thead>
<tbody>
<tr>
<td>Complete resection (%)</td>
<td>100</td>
<td>100</td>
<td>85</td>
<td>42</td>
</tr>
<tr>
<td>Recurrence (%)</td>
<td>1</td>
<td>4</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>5-Year survival (%)</td>
<td>100</td>
<td>98</td>
<td>89</td>
<td>71</td>
</tr>
</tbody>
</table>

From Kondo et al

Diagnostic Pathway

- Baseline bloods including FBC, renal and liver function tests
- Optional bloods include TFTs, β-HCG and AFP (as per MDT decision)
- Pulmonary function tests. Ideally should include gas transfer, lung capacity and six minute walk test (6MWT); not only spirometry
- CT chest and abdomen with contrast
- PET CT and/or Octreoscan optional (decide at MDT)
- PET CT can be useful in patients with myasthenia gravis to differentiate between thymic hyperplasia and thymoma when CT findings are unequivocal. PET CT is also useful in selected follow-up cases complimenting CT findings (MDT decision). Octreoscan is also sometimes useful in detecting relapses (MDT decision).
- MRI may be helpful in demonstrating vascular invasion if CT findings are suspicious (MDT decision).
- Any symptoms or signs of myasthenia gravis should prompt referral to a Consultant Neurologist with an interest in the condition. This may have important anaesthetic implications.
If the likelihood of thymoma is felt to be high at the Multi-disciplinary team (MDT) meeting and the tumour appears to be well encapsulated (i.e. stage I), then proceeding to surgery for complete excision without biopsy is a reasonable option.

The risk of tumour seeding from core needle biopsy has been reported as negligible and this should not therefore not deter the MDT from requesting a pre-op histological diagnosis.

Other options for obtaining a histological diagnosis include anterior mediastinotomy (Chamberlain procedure) and video-assisted thoracic surgery (VATS) biopsy, especially if pleural metastases are suspected.

Histopathology should be reviewed by a pathologist with an interest in this disease.

**Follow-up imaging**
Because of the high relapse rates in stage 3 & 4 cases further regular follow-up with CT (additional PET CT or Octreoscan in selected cases) is suggested. Follow up CT scanning may also be appropriate for patients who decline post-operative radiotherapy for close resection margins.

**Management**
All patients should be discussed in the regional lung cancer MDT. Thymic tumours are uncommon and there is a lack of data in the literature to make firm management recommendations. This document offers guidance based.

**Resectable disease**
*Surgical Approaches*
Thymectomy should involve the en bloc removal of the tumour and all of the thymus. This may require the removal of lung, pericardium, left brachiocephalic vein, one phrenic nerve, SVC and even the aorta with the specimen. The value of a debulking procedure is controversial.
Resection can be performed via sternotomy, a limited upper sternotomy, a transcervical approach or using video-assisted thorascopic surgery. Some texts recommend that the transcervical approach should only be used for myasthenia gravis patients without a thymoma. The final choice of approach depends on the CT findings, the surgeon’s preference and the patient’s preference.

All post-operative cases should be discussed again at the MDT to decide on potential further management options.

No further treatment is required for completely resected tumours with no capsular invasion.

In patients with complete R0 resection, but with capsular invasion, the role of adjuvant radiotherapy is unclear. In general, the higher the WHO grade, the higher the risk of recurrence. Ideally this pros and cons of radiotherapy should be discussed with the patient. An alternative option is surveillance CT scanning, as salvage surgery or radiotherapy may offer the chance of long term cure

R1 resections warrant referral for a discussion of post-operative radiotherapy.

R2 resections warrant referral for a discussion of post-op radiotherapy and chemotherapy, although no firm recommendations can be made.

**Masaoka Stage III and borderline resectable disease.**

The option of neoadjuvant chemotherapy should be discussed at the MDT. No firm recommendation can be made regarding chemotherapy*, due to lack of trial evidence, but a reasonable option is to offer 3-4 cycles and re-discuss at the MDT following repeat imaging.

Patients that do undergo resection are likely to require post-op radiotherapy.

(* see Appendix 1)
Unresectable and metastatic disease

Patients with good performance status should be offered chemotherapy. Some patients may then be candidates for radiotherapy or possibly surgery depending on response and stage. Further discussion at the MDT should be considered following completion of chemotherapy and re-imaging.

Recurrent disease

Patients with local recurrence may be candidates for salvage surgery or radiotherapy. The role of chemotherapy should also be discussed in this setting.

Patients with metastatic disease should be considered for chemotherapy and palliative radiotherapy.
The Role of Thymectomy in the management of Myasthenia Gravis.

The severity of myasthenia gravis has been classified using the Modified Osserman Classification for Myasthenia Gravis – see table.

*Modified Osserman Classification for Myasthenia Gravis*

<table>
<thead>
<tr>
<th>Class</th>
<th>Distribution of Symptoms</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>Ocular</td>
</tr>
<tr>
<td>II</td>
<td>Mild general weakness, usually with ocular muscle weakness</td>
</tr>
<tr>
<td>III</td>
<td>Predominantly bulbar involvement, usually with mild general weakness</td>
</tr>
<tr>
<td>IV</td>
<td>Moderate generalised weakness</td>
</tr>
<tr>
<td>V</td>
<td>Severe generalised weakness</td>
</tr>
</tbody>
</table>

A thymoma is present in 10-20% of patients with myasthenia gravis. The benefits of thymectomy were first recorded in 1910. 80-90% of patients with myasthenia gravis improve by at least one Osserman classification following thymectomy. 50-70% of these patients have drug free remission after thymectomy.

A review of the available literature reveals that the indications for thymectomy in myasthenia gravis vary between units. Thymectomy should be considered in patients with

- Osserman class II – V disease
- Osserman class I disease refractory to medical treatment
- All patients with a thymoma. The presence of a thymoma correlates with a poorer response to thymectomy compared to those who have a thymectomy without the presence of a thymoma.

The anaesthesia for thymectomy involves the minimal use of muscle relaxants and opiates. Anticholinesterases should be continue post operatively and managed by the patient's neurologist as an outpatient.
Thymoma Appendices

Thymoma Appendix 1

Suggested First Line Chemotherapy regimens

There are no randomised phase III trials in this disease so no firm recommendations can be made. However there is a significant amount of data in the literature supporting the use of the following regimens:

CAP – Cyclophosphamide 500mg/m\(^2\) (day 1), Adriamycin (doxorubicin) 50mg/m\(^2\) (day 1), Cisplatin 50mg/m\(^2\) (day 1). Administered every 3 weeks.

PE- Suggest as per small cell chemotherapy protocols, but the following schedule has also been used:

Cisplatin 60mg/m\(^2\) (day 1), Etoposide 120mg/m2 (day 1-3). Administered every 3 weeks.

ADOC - Cisplatin 50mg/m\(^2\), Adriamycin (doxorubicin) 40mg/m\(^2\) (day 1), Vincristine 0.6 mg/m\(^2\) (day 3), Cyclophosphamide 700mg/m\(^2\) (day 4). Administered every 4 weeks.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Patients</th>
<th>CR</th>
<th>PR</th>
<th>Response rate (%)</th>
<th>Median survival (y)</th>
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</thead>
<tbody>
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<td>Cisplatin, doxorubicin, cyclophosphamide (PAC)</td>
<td>30</td>
<td>3</td>
<td>12</td>
<td>50</td>
<td>3.2</td>
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<tr>
<td>Cisplatin, doxorubicin, vincristine, cyclophosphamide (ADOC)</td>
<td>32</td>
<td>15</td>
<td>14</td>
<td>90</td>
<td>1.25</td>
</tr>
<tr>
<td>Cisplatin, etoposide (PE)</td>
<td>16</td>
<td>5</td>
<td>4</td>
<td>56</td>
<td>4.3</td>
</tr>
<tr>
<td>Etoposide, ifosfamide, cisplatin (VIP)</td>
<td>28</td>
<td>0</td>
<td>9</td>
<td>32</td>
<td>2.6</td>
</tr>
<tr>
<td>Octreotide</td>
<td>38</td>
<td>0</td>
<td>4</td>
<td>10.5</td>
<td>3.8</td>
</tr>
<tr>
<td>Octreotide + prednisone</td>
<td>21</td>
<td>2</td>
<td>6</td>
<td>38</td>
<td>Not reached</td>
</tr>
</tbody>
</table>

(From Loeherer, Fornasiero, Giaccone)
Thymoma Appendix 2

Suggested 2nd line regimens

- Octreotide and prednisilone
- PE or Carboplatin/Etopside
- Etoposide

Thymoma Appendix 3

Radiotherapy

Due to lack of clinical trials, there is no gold standard for the use of radiotherapy in the curative, adjuvant or palliative settings. An individual case based approach should be taken.

Suggested regimens for radical radiotherapy:

- 60-66 Gy in 30-33 fractions
- 50-55 Gy in 20 fractions

Suggested regimens for Adjuvant radiotherapy:

- 50Gy in 25 fractions
- 40Gy in 15 fractions
Thymoma References


Giaccone G. Treatment of malignant thymoma. Curr Opin Oncol 2005;17(March (2)):140—6


Referral Guidelines

All the constituent MDT’s within the North of England Cancer Network recognise that referral to another MDT, or specialist centre for specific treatment might be necessary. Examples of such treatment might include major airway stenting, radical surgery for mesothelioma.

When a local MDT or cancer team feel that such referral is indicated then the following are agreed:

- The MDT will follow the pathology guidelines regarding specialist MDT referral
- The MDT will provide all data to the receiving MDT including radiology, pathology and clinical information.
- The clinician in charge of the patient or a responsible member of their team will write a formal referral letter to the receiving team.

On return of the patient the specialist MDT team will be expected:

- To provide written information regarding the treatment delivered
- Indicate the need for any follow up
- Contact the primary team on discharge

At all times the members of the North of England Cancer Network agree to the need for comprehensive and good communication.
Sources of Information and Patient Support Groups

**Roy Castle Lung Foundation**
Patient Support and Information Network
Tel: 0800 358 7200

**Cancer Support Service Cancer Backup**
Tel: 0207 696 9003

**British Lung Foundation – Breathe North**
Tel: 0191 2630276

**National Mesothelioma Resource Centre**
Tel: 0800 1692409

**Macmillan Cancerline**
Tel: 0808 808 2020

For patients and carers who are able to travel to Newcastle, a Lung Cancer Support and Information Group has been set up at the **Northern Centre for Cancer Care**
Telephone number 0191 2138608

**North Tees Lung Cancer Support Group:**
First Monday in the month (excluding Bank Holidays), 2:00pm – 4:00pm
Lung Health Seminar Room, within the University Hospital of North Tees
For further details contact: Macmillan lung Cancer Nurse Specialists
Tessa Fitzpatrick or Jeanette Draffan - 01642 624106

**South Tees Lung Cancer Support Group**
First Wednesday of every month; 5:30pm – 7:30pm
Education Centre, James Cook University Hospital
For further details contact: Macmillan Lung Cancer Nurse Specialists Stacey Stockdale or Pauline Featonby – 01642 282526
Darlington Lung Cancer Support Group
Last Tuesday of every month; 2:00pm – 4:00pm
Blackwell Grange Hotel, Darlington
For further details contact: Respiratory Oncology Nurse Specialist
Delphine Brown - 01325 743424

Bishop Auckland Lung Cancer Support Group
First Wednesday of every month; 2:00pm – 4:00pm
For further details contact: Respiratory Oncology Nurse Specialist
Karen Capenhurst - 01388 455784

Sunderland Lung Cancer Support Group
First Thursday of every month; 5:30pm – 7:30pm
Education Centre, Sunderland Royal Hospital
For further details contact: Macmillan Lung Cancer Nurse Specialists
Sue Pollock or Joanne Anderson - 0191 5656256
www.sunderlandlungcancersupportgroup.co.uk

Freeman Hospital Lung Cancer Support Group
First Monday of every month; 2:00pm – 4:00pm
Disability North, Dene Centre, Castle Farm Road, Gosforth
For further details contact: Lung Cancer Nurse Specialists
Claire Donaldson or Christine Rushton – 0191 224 4856
Continuing Care

- Before discharge from hospital the consultant and the nursing staff should ensure that the patient and carers have been given all the information about their condition and its treatment that they wish to know.

- They should be referred to the Lung Cancer Nurse Specialist, who if at all possible, should meet with the patient and family/carer prior to discharge or very shortly after.

- Information should be given to the patient in the company of a spouse, relative or friend if possible. A record should be made in the case notes of the information given, and this information should be made available to the general practitioner.

- All patients should be referred to the District Nursing Service regardless of their needs to continue to care in the community.

- If the patient is in need of symptom control/Palliative care then the appropriate referral should be made to the Macmillan team and/or Palliative Care team.

- A Referral to the Hospice could be sought after discussions with the patient for further support/care i.e. Day Support, Respite, End of Life care.

- Patients should be aware of who to call for urgent problems and how best to contact them. Cancer units and centres should begin to name a key worker for every patient.

- The patient’s wishes should be sought when there are major decisions to be made about changes in care pattern. Any changes should be made known to the General Practitioner.
Follow Up:

- Ideally follow up might be supervised in a multi-disciplinary clinic with input available from respiratory and palliative care physicians, oncologists, lung cancer specialist nurses and other Multiprofessional team members such as Dietitian, Physiotherapist, Occupational Therapist, Social Worker etc. It is acknowledged that lack of personnel may preclude such an arrangement in some units.

- Hospital follow up should be continued whilst there is a reasonable prospect of hospital treatment or specialist advice being needed. It may also be appropriate to continue hospital follow up in other circumstances, for instance where this is perceived to be important to sustain a patient's morale or where follow up is necessary for the purpose of a clinical trial.

- Hospital follow-up may be in a nurse-led clinic.

- An explicit follow up policy should be developed for each patient, taking note of the wishes and interests of the patient and general practitioner. It should be clear to the patient and general practice who is supervising follow up i.e. who to contact if problems arise.

- Follow up in multiple clinics should be avoided.
Supportive Care and Palliative Care

Attention needs to be paid to patients’ symptoms and concerns in all respiratory disease, but this is particularly true in lung cancer where, in the majority of cases, the patient will die from the condition. Below are listed definitions of approaches to this type of care.

- **Palliative care**: It is an approach that focuses on the total care of the patient and family who are facing life-threatening illness. It embraces symptom control, psychological, social, and spiritual support and aims to optimise quality of life in those with an incurable illness. This type of care should be offered by all healthcare professionals.

- **Specialist palliative care**: It is care provided by clinicians who have specialist training and skills in palliative medicine, working within specialist multidisciplinary teams.

- **Supportive care**: It is a broader concept, which includes the provision of support and palliation to patients at an earlier stage of their illness when outcomes, such as cure, are still possible.

- **End of Life Care**: An approach that enables the supportive and palliative care needs of both patient and family to be identified and met throughout the last phase of life and into bereavement.

- **Key features of end of life care**:
  - Anticipation and management of deterioration in the patient’s condition
  - Advance care planning in accordance with patient preferences
  - Patient choice about place of care and death
  - Effective co-ordination of care across all teams and providers of care (in statutory, voluntary and independent sectors) who are involved in the care of patient and family
Care of the Dying: Care of the patient and family in the last hours and days of life.

- Incorporates four key domains of care, physical, psychological, social and spiritual
- Supports the family through this phase and into bereavement.
- This is often documented and supported by use of the Liverpool Care Pathway (LCP)

Supportive care

- The need for supportive care will vary immensely between patients. The principle is that all patients and their families should be offered support as early in their cancer journey as is needed, even if they may be going to have potentially curative treatment.

- Supervision of supportive care is the responsibility of the relevant general practitioner (GP) and/or hospital specialist, depending on the needs of the particular patient. If the patient is undergoing active anti-cancer treatment, then it is likely that this will be coordinated by the hospital Clinical Nurse Specialist (CNS).

- Patients receiving supportive care should have regular follow up by their GP, respiratory physician, oncologist or CNS, depending on the circumstances and the wishes of the patient and their carers.

- Although supervision of supportive care may be undertaken by the professionals listed above, immediate liaison with the patient may be best conducted by a district nurse (DNS). The patient and his/her carers should be aware of the names of both the doctor and nurse responsible for their care.

- Supportive care includes:
  - Self help and support
  - User involvement
Information giving
Psychological support
Symptom control
Social support
Rehabilitation
Complementary therapies
Spiritual support

Palliative care

- In patients in whom curative treatment is not possible, palliative care becomes more relevant. All healthcare professionals should offer this.

- If the needs cannot be met by the hospital clinical team, GP or DNS then the patient should have access to specialist palliative care.

- Specialist palliative care teams are now available throughout the North of England Cancer Network in both community and hospital, with the backup of specialist palliative care inpatient hospice beds in most areas.

- Help can vary from telephone advice (often available out of hours from hospices), single visits (domiciliary, out patient or ward consultation), to regular community involvement or an inpatient admission to a specialist palliative care hospice bed.

The role of specialist palliative care early after diagnosis

In a study from the USA, Temel described how early input from specialist palliative care (SPC) could improve symptom control and facilitate decision making about treatment preferences. More surprisingly, the group randomised to receive this support lived longer. This led to the recommendation that early specialist palliative care should be offered to all new lung cancer patients. It must be said however that the organisation of lung cancer services in the UK
is different, and here the lung CNS will fulfil some of roles undertaken by SPC in the Temel study.

Network wide guidelines exist for the management of certain core symptoms and situations in palliative care. These have been incorporated into a small A5 sized booklet and are distributed across the network. They are also available on the North of England cancer network website where other guidelines and links will be available: http://www.nescn.nhs.uk/

Supportive and Palliative Care References


North of England Lung Cancer Teams

North of England Cancer Network Lung Cancer Physicians, supporting non-surgical Oncologists, supporting Cardiothoracic Teams and Lung Cancer Clinical Nurse Specialists in the cancer units are as follows:

### SOUTH TEES HOSPITALS ACUTE NHS TRUST:

<table>
<thead>
<tr>
<th>Chest Physician</th>
<th>Clinical Nurse Specialist</th>
<th>Oncologists</th>
<th>Thoracic Surgical Team</th>
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</thead>
<tbody>
<tr>
<td><strong>James Cook University Hospital, Middlesbrough</strong></td>
<td></td>
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</tr>
<tr>
<td>Dr. V. Dudzevicious</td>
<td>Jan Keld</td>
<td>Dr. C. Peedell</td>
<td>Mr. Jonathan Ferguson (Key Surgeon)</td>
</tr>
<tr>
<td>Dr. G. Antunes</td>
<td>Sarah Clarkson</td>
<td>Dr Shakespeare</td>
<td>Mr. Joel Dunning</td>
</tr>
<tr>
<td>Dr. Mustafa</td>
<td>Andrea Lynas- Clinical SR</td>
<td>Dr. N. Wadd (brachytherapy)</td>
<td>Mr. Simon Kendall</td>
</tr>
<tr>
<td>Dr. N. Krishnaraj</td>
<td>Tel no: 01642 282526</td>
<td>Dr. Van der Voet</td>
<td>Thoracic Nurse Specialists</td>
</tr>
<tr>
<td>Dr. Sathyamurthy</td>
<td>Bleep 0769625012</td>
<td>Dr. E. Aynsley</td>
<td>Leanne Connelly</td>
</tr>
<tr>
<td></td>
<td>Emails:</td>
<td>Dr. S. Lawless</td>
<td>Rachel Calvert</td>
</tr>
<tr>
<td></td>
<td><a href="mailto:Jan.Keld@stees.nhs.uk">Jan.Keld@stees.nhs.uk</a></td>
<td>Dr F Azribi</td>
<td>Emails:</td>
</tr>
<tr>
<td></td>
<td><a href="mailto:Sarah.Clarkson@stees.nhs.uk">Sarah.Clarkson@stees.nhs.uk</a></td>
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<td><a href="mailto:leanne.connelly@stees.nhs.uk">leanne.connelly@stees.nhs.uk</a></td>
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<td></td>
<td><a href="mailto:andrea.lynas@stees.nhs.uk">andrea.lynas@stees.nhs.uk</a></td>
<td></td>
<td><a href="mailto:Rachel.calvert@stees.nhs.uk">Rachel.calvert@stees.nhs.uk</a></td>
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</table>

| **The Friarage Hospital** | | | |
| Dr. D. Spence | Sarah Clarkson | Dr. C. Peedell | Mr. Jonathan Ferguson (Key Surgeon) |
| | Tel No: 01609 764211 | Dr Shakespeare | Mr. Joel Dunning |
| | Email: Sarah.Clarkson@stees.nhs.uk | Dr. N. Wadd (brachytherapy) | Mr. Simon Kendall |
| | | Dr. Van der Voet | Thoracic Nurse Specialists |
| | | Dr. E. Aynsley | Leanne Connelly |
| | | Dr. S. Lawless | Rachel Calvert |
| | | Dr F Azribi | Emails: |
| | | | leanne.connelly@stees.nhs.uk |
| | | | Rachel.calvert@stees.nhs.uk |

### NORTH TEES & HARTLEPOOL FOUNDATION NHS TRUST:

<table>
<thead>
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# COUNTY DURHAM AND DARLINGTON HOSPITALS FOUNDATION TRUST:

## Darlington Memorial Hospital

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<thead>
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<th>Chest Physician</th>
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</table>
| Dr. R. Abassi  
Dr.Wyn-Jones (Mat Leave)  
Dr I Molyneaux  
Dr.P.De (Associate Specialist) | Delphine Brown  
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# NORTH CUMBRIA ACUTE HOSPITALS NHS TRUST:

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### West Cumberland Hospital (Whitehaven)

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<tr>
<th>Dr Ting (Locum)</th>
<th>Vicky Lamonby</th>
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<td>Tel No: 01946 693181</td>
<td>Email: <a href="mailto:Vicky.Lamonby@ncuh.nhs.uk">Vicky.Lamonby@ncuh.nhs.uk</a></td>
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### Cumberland Infirmary Carlisle

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<tr>
<th>Dr M Hewson</th>
<th>Kim Robinson</th>
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### CITY HOSPITALS SUNDERLAND NHS FOUNDATION TRUST

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<td>Dr I Taylor</td>
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<td>Dr H Clague</td>
<td>Tel No: 0191 5656256 Ex 47521</td>
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<tr>
<td>Dr K Sridharan</td>
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<tr>
<td>Joanne Anderson</td>
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<td>Bleep 52237 via switchboard</td>
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<td>Dr Chris Jones</td>
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### NEWCASTLE UPON TYNE HOSPITALS NHS FOUNDATION TRUST

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<td>Dr B Higgins</td>
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<tr>
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| RVI |
| Dr A Ward | Vicki Anderson |
| Dr I Forrest | Tel: 0191 2821875 |
| Dr J Gardiner (Medical Oncologist) | Thoracic Nurse Specialist |
| Jackie Trinder |
### GATESHEAD HEALTH NHS FOUNDATION TRUST

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### SOUTH TYNESIDE NHS FOUNDATION TRUST

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<tr>
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### NORTHUMBRIA NHS FOUNDATION TRUST

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<td>Mr S Barnard Mr S Clark Mr S Stamenkovic Mr J Forty Thoracic Nurse Specialist Jackie Trinder Email: <a href="mailto:Jackie.Trinder@nuth.nhs.uk">Jackie.Trinder@nuth.nhs.uk</a></td>
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Pathology Guidelines for the Examination and Reporting of Lung Cancer Specimens

Introduction

These guidelines for the examination and reporting of lung cancer specimens are supplementary to the following national guidance:

- Minimum dataset for lung cancer histopathology reports issued by the Royal College of Pathologists (3rd edition 2011).
- Tissue Pathways for Pulmonary Pathology issued by the Royal College of Pathologists (2008).

All lung cancer cases should be reviewed by a Lung Cancer multidisciplinary team. There should be a nominated Lead lung pathologist for the service but all pathologists reporting lung cancer specimens should participate in lung MDT/CPC meetings, in an appropriate EQA scheme and in local audit (including an assessment of consistency of reporting, as appropriate to the site). If there is a significant discrepancy with the clinical/radiological findings the pathological material from diagnostic lung specimens should be reviewed, if possible by a second pathologist with an interest in lung cancer.

Specimens should be reported to an agreed timeframe so as to allow appropriate clinical decision making at a planned lung MDT meeting.
Specimen Types

Diagnostic:
Bronchial biopsies
Pulmonary cytology (brushings, washings, transbronchial FNA etc)
Needle core biopsy
VATS biopsy/Open lung biopsy
Mediastinal biopsy
Lymph node biopsy
Pleural biopsy
Pleural fluid cytology
Frozen sections

Therapeutic:
Segmentectomy (VATS or open)
Lobectomy (VATS or open)
Sleeve resection
Pneumonectomy (intra or extra pericardial)
Chest wall resection
Pleurectomy
Pleuropneumonectomy
Metastasectomy

Specimen Examination

Each pathology service should establish a defined protocol for each type of diagnostic and therapeutic lung specimen type received by the laboratory, taking into account the above guidance. The protocols should be regularly reviewed and updated by the Lead lung pathologist in consultation with other pathologists who participate in service delivery.

Access to specimen radiography and specialist radiological opinion should be available for relevant cases.

Lung tissue should only be removed and stored for the purposes of research if it is surplus to the requirements of the diagnostic process. Appropriate patient consent and ethical approval should be obtained.
Minimum Dataset For Reporting

Diagnostic specimens:

For lung

- Tumour type (small cell or non-small cell; *if NSCLC further tumour subtyping for patient tailored therapy whenever possible is also required, along with due consideration also for conservation of suitable tumour material for molecular testing*).

For pleura

- Tumour type

Therapeutic resections:

- Relevant RCPath Dataset with local modifications
- Specimen type (or procedure where relevant)
- Laterality
- Specimen dimensions
- Location of tumour
- Tumour size
- Distance from bronchial or other relevant resection margin
- Extent of atelectasis or obstructive pneumonitis
- Tumour type
- Tumour grade
- Local invasion (pleura, chest wall, mediastinal structures etc)
- Lymph node spread (by node station group)
- Resection margins (bronchial, mediastinal, vascular and chest wall)
- Other relevant pathology
- TMN staging system

Departments and MDTs should work towards recording and storing the dataset items as individually categorised items in a relational database, so as to allow electronic retrieval and to facilitate the use of pathology data in clinical audit, service planning and monitoring, research and quality assurance.
Laboratories should use an agreed diagnostic coding system (e.g. SNOMED). All malignancies must be reported to the Northern and Yorkshire Cancer Registry, in accordance with the service level agreement with their host Trust.

**Grading and Staging Conventions**

Tumour grading:
- WHO invasive carcinoma grade system

Tumour staging:
- TNM classification of malignant tumours (*7th edition*)
Use of Ancillary Laboratory Techniques

All laboratories providing a Pathology service in the network must have at least conditional laboratory (eg CPA) accreditation and ensure participation in an appropriate external quality assurance programme which demonstrates satisfactory laboratory performance.

**Tissue conservation should be exercised in view of expanding indications for molecular testing.** If sectioning small biopsies at multiple levels is required, care should be taken to ensure that adequate numbers of spare sections are retained to allow immunostaining of tumour that may “cut out” in the deeper levels.

Immunohistochemical procedures which may be of value include the following:

<table>
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<tr>
<th>Diagnostic scenario</th>
<th>Immunohistochemical markers</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Neuroendocrine Differentiation</td>
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<td>Chromogranin</td>
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<tr>
<td>Primary or metastatic Carcinoma</td>
<td>TTF-1, ER, CK7, CK20, CA125, PSA, CA19-9, S100, Melan A, CD15, thyroglobulin</td>
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<tr>
<td>Adenocarcinoma v Mesothelioma</td>
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<tr>
<td>Small cell carcinoma v Lymphocytes/lymphoma v metastatic tumour</td>
<td>CD56, CD45, Cytokeratins, TTF1</td>
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Audit

All pathologists reporting lung cancer specimens should participate in a relevant EQA scheme and in local audit (including an assessment of consistency where more than one pathologist participates in service provision). Audit may take the form of:

- review of compliance with procedures for specimen examination and reporting
- completeness of datasets
- systematic logging of diagnostic agreement/disagreement during review of cases for MDTMs
- review of diagnostic consistency between pathologists using data from cases in EQA circulations or blind circulations.

The results of the audit process should be discussed with all pathologists who participate in service delivery and used to inform the development of reporting protocols.
Referral for Review or Specialist Opinion

Referral for treatment

All patients referred for treatment at a hospital within the North of England Cancer Network following diagnosis elsewhere must be reviewed and discussed at the treating hospital’s multidisciplinary team meeting (MDTM).

The complete diagnostic pathology report must be available at the MDTM, and where considered relevant, the histological/cytological material should be reviewed. Situations when review is important include when there is a significant discrepancy with the clinical/radiological findings, or when the original pathologist expressed diagnostic uncertainty or when a rare type of tumour is diagnosed. Pathological material should be requested at least 5 working days before and received at least 3 working days before the relevant MDTM to allow sufficient time for review.

A formal report should be issued by the reviewing pathologist to the responsible clinician at the treating hospital. The results of the review should be sent to the original pathologist, either by copy of the review report or by letter.

Where patients have been referred for oncology treatment, requests for specialist biomarker studies will be co-ordinated between the treating oncology service, their local pathology service and the referring hospital’s pathology service, as appropriate. The oncology service must agree a mechanism for requesting tests and the relevant pathological material with their local pathology service. Requests for pathological material should be made in good time to ensure that results are available at the MDTM where the patient is to be discussed.
Referral for Specialist Opinion

All lung lymphomas should be referred to the Haematological Malignancy Diagnostic Service for phenotypic analysis and confirmation of diagnosis.

In cases of diagnostic difficulty, referral will usually be made to the lead pathologist of the relevant specialist MDT in the network, although referral to other specialists within or out with the network may be appropriate in individual cases. Cases referred for individual specialist or second opinion will be dealt with by the individual pathologist and a report issued by them. Where relevant, tissue blocks should be made available to allow any further investigations that are deemed appropriate. The result of the review should be communicated to the referring pathologist by letter and also by fax/telephone as appropriate.

In instances when the patient is referred for an opinion by a specialist multidisciplinary team the case should be referred to the Lead Pathologist of the appropriate MDT and dealt with according to specialist team/Cancer Centre MDT guidelines.
Pathology References


*Tissue Pathways for Pulmonary Pathology issued by the Royal College of Pathologists* (2008).


Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart (IARC/World Health Organization Classification of Tumours) Travis W D, Brambilla E, Muller-Hermelink HK, Curtis C WHO (2004)

Guidelines on inter-departmental dispatch of samples from patients sent to another hospital or centre for assessment and/or treatment. The Royal College of Pathologists (2004)

NICE. Lung cancer: the diagnosis and treatment of lung cancer (February 2005)

These guidelines were initially developed by Dr Fiona Black in 2005 on behalf of the Histopathology Group of the Northern Cancer Network and histopathologists in the Northern Cancer Network. They were agreed by the Histopathology Group of the Northern Cancer Network. The group are indebted to the Pathology Group of the Yorkshire Cancer Network who kindly agreed to allow us to adopt, with modifications, their original document. These guidelines have subsequently been imported into the current North of England Cancer Network Guidelines with very minor formatting changes carried out by Dr Leitch Chair Lung NSSG June 2009.
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General Guideline References


The Royal College of Radiologists, Issue 2, August 2006: Recommendations for Cross Sectional Imaging in Cancer Management, Issue 2,
Appendix 1- Summary of Lung Cancer Imaging - as submitted to the Radiology group

IMAGING GUIDELINES FOR LUNG CANCER.

A. Diagnosis
1. Primary Care- referral for Chest X-ray
2. Specialist Unit
3. Unexpected finding of suspected cancer.

B. Staging.
1. Non small cell lung cancer.
2. Small cell lung cancer.

C. Follow up.

A. Diagnosis

1. Primary Care- referral for Chest X-ray

An urgent referral for a chest X-ray should be made when a patient presents with:

- Haemoptysis or
- Any of the following unexplained persistent (> 3 weeks) symptoms or signs
  - Chest and or shoulder pain
  - Dyspnoea
  - Weight loss
  - Chest signs
  - Hoarseness
  - Finger clubbing
  - Cervical or supraclavicular lymphadenopathy
  - Cough with or without any of the above
- Features suggestive of a metastasis from lung cancer (e.g. brain, bone, liver or skin).

In addition, investigations should be arranged for those with chronic lung disease where there is a change in symptom complex e.g. changed cough in COPD / fibrosis.

A report should be made to the primary healthcare professionals within 5 days of the referral for a chest X-ray.

It should also be noted that a CXR may be normal despite the presence of cancer and where there is clinical suspicion then a normal CXR should not be taken as false reassurance.

2. Specialist Unit.

Only half of patients referred to a clinic with suspected lung cancer will turn out to have this pathology. Investigation therefore has diagnostic and staging goals. In order to prevent unnecessary delay these may be combined but care should be taken to ensure that the pathway is tailored to the individual patient to minimise unnecessary investigations. CT imparts a significant radiation dose and contrast has a small but significant morbidity and mortality.

If a patient presenting to a specialist unit with suspected Lung Cancer has not had a Chest X-ray this should be performed at the time of the first visit.

When a patient with suspected cancer is seen in the clinic then they should be offered a CT as an initial investigation to further the diagnosis and stage the possible disease.

This CT scan should be performed before:
  - An intended fibreoptic bronchoscopy
  - Most other biopsy procedures.
Local consideration should be made to specific arrangements in the investigation pathway such that the results of CT are available before deciding on the most appropriate next management step. For example, pre-arranged CT slots shortly after an initial clinic visit with rapid review of the patient. For example, CT before a clinic appointment provided this does not lead to unnecessary CT scans or delay in referral. Where there is a CT scan before a clinic appointment then there should be appropriate discussion with the patient.

If the chest x-ray shows a mass a combined diagnostic/staging scan should be performed including the liver and adrenals (see protocol below). If however there is no definite evidence of cancer, e.g. normal chest x-ray, a CT scan of the chest alone may be sufficient to exclude or confirm a lesion. Contrast is not usually necessary but may be used if there is uncertainty or the Radiologist is not confident reporting non-contrast scans. If the chest scan shows a lesion a full staging scan should be performed at the same attendance. If contrast has been given the liver and adrenal phase may be set up before the chest scan so the scan can be continued immediately.

It is recognised that in some units a Radiologist is not always present when the scan is performed and the decision to do a diagnostic study or combined diagnostic and staging scan will need to be made at the time of protocolisation.

3. Unexpected finding of suspected cancer.

If a CXR has been performed and an incidental suspected cancer identified then a second copy of the radiologist’s report should be sent to a designated member of the Multidisciplinary team (MDT) usually the respiratory physician. The MDT should have a mechanism to ensure that there is follow up of these reports to ensure a management plan has been instituted by the patient’s GP.
B. Staging:
1. Non Small Cell Lung Cancer

CT of the chest and abdomen is the investigation of choice to stage the primary tumour and to detect metastatic disease. Post contrast CT of the brain should be included in the initial staging if symptoms are present or if curative therapy, including surgery, radiotherapy, chemotherapy or a combination, is being considered.

If any such patient has not had a head scan at the initial staging it should be performed separately before treatment.

MRI is the investigation of choice if the CT is normal in the presence of neurological signs.

Staging CT should include post-contrast scans through the chest (to include supraclavicular fossae) and upper abdomen (to include liver and adrenal glands). 100-150mls of intravenous iodinated contrast should be injected at 3-4ml/sec. The chest should be scanned during the arterial phase (20-30 sec delay), and the abdomen during the portal venous phase (60-70 sec delay).

CT may not provide complete staging and other techniques e.g. ultrasound may be considered.

Pancoast (superior sulcus) tumours are best visualised by multiplanar reconstructions, however the extent of these tumours is best demonstrated by MRI.

An 18F-deoxyglucose positron emission tomography CT (FDG PET-CT) scan should be performed to stage disease in any patient who at diagnosis or after down staging is to be offered radical treatment, surgery, radiotherapy, chemotherapy or a combination. Most cases will be for NSCL. It may also be used in cases of indeterminate chest mass—where biopsy is difficult or has failed.
Local arrangements should be in place with consideration given to concurrent investigation of suspected abnormalities such that tests are done in parallel rather in series. E.g. A patient with a potentially operable tumour might have CT biopsy and FDG-PET requested in parallel.

Where metastatic disease is considered then CT, radiography, bone scan or MRI should be requested as necessary.

All patients who are candidates for thoracotomy should have a staging CT scan and a separate PET scan. The images should be available at the time of consultation with the thoracic surgeon.

2. Small Cell Lung Cancer
SCLC should be staged primarily with CT and imaging of any symptomatic area. The scan should cover the chest and abdomen as above and should include the head. (See PET-CT above).

C. Follow-up
Repeat staging should be undertaken after downstaging with chemotherapy prior to surgery. Repeat staging is also required for patients who develop symptoms of SVC obstruction.

If response to treatment such as chemotherapy cannot be assessed adequately by CXR repeat CT scans may be required.

At the end of a treatment programme repeat staging may be necessary to plan further management.

If the patient develops new or recurrent symptoms targeted imaging should be performed. Formal restaging may also be required.

If PET-CT is used to assess residual disease then a gap of at least 6 weeks should be left after chemotherapy.
NECN CHEMOTHERAPY TREATMENT ALGORITHM FOR LUNG

“Quality and safety for every patient every time”

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For more information regarding this document, please contact:

NSSG Chair: Dr L Mitchell
INTRODUCTION

The 2011 Peer Review Chemotherapy Measures require each Network Site Specific group (NSSG) to agree in consultation with the Network Chemotherapy Group (NCG) a set of site specific chemotherapy treatment algorithms for the Network.

Peer Review Definitions

Chemotherapy treatment algorithm
A guideline which specifies the acceptable ranges of regimen options for named steps on the patient pathway. Treatment algorithms are cancer site-specific. Thus, the treatment algorithm for the Lung NSSG includes a statement of the range of regimens agreed as acceptable.

Chemotherapy
The term 'chemotherapy' refers to the use of those cytotoxic agents commonly understood and accepted as being covered by this term and includes other agents such as, biological therapy and small molecule tyrosine kinase inhibitors used for the systemic treatment of cancer.

In NECN Treatment Algorithms are included in each NSSG’s Clinical Guidelines which can be found under the tumour specific page of the guidelines section of the website, e.g. for Lung Cancer http://www.nescn.nhs.uk/group/lung-nssg/

SUPPORTING DOCUMENTS

As new regimens are approved by NICE / NECDAG protocols for use of the new treatment will be uploaded to the chemotherapy site specific pages. The NSSG will be asked to update their algorithm with each new treatment approval.
The availability of the Cancer Drug Fund (CDF) has increased the number of treatments potentially available to patients. CDF funded drugs may not be included in the NSSG clinical guidelines due to the dynamic nature of CDF funding (i.e. treatments can be removed as well as added).

Any deviation from the algorithm should be recorded by the local Trust clinical chemotherapy service and brought to the NCG for discussion. The Network Policy on managing deviations from approved protocols/ algorithms is on the website: [http://www.necn.nhs.uk/chemotherapy-documents/](http://www.necn.nhs.uk/chemotherapy-documents/)

**LIST OF APPROVED REGIMENS**

The NECN website provides the most up to date list of approved regimens and should be regularly checked. Appendix One below summarises the Lung regimens on the website.

**LUNG ALGORITHM**

**Chemotherapy General Principles**

- Consideration should be given in the first instance as to whether or not chemotherapy is appropriate for the individual. This decision will be based on the extent and type of disease as well as performance status and will take into account the individual wishes of the patient.
- The aim of the chemotherapy (curative, neoadjuvant, adjuvant or palliative) should be defined prior to administration and this should be discussed with the patient together with the potential side effects of the treatment.
- Chemotherapy should be administered in accordance with the published recommendations of the JCCO using whenever possible protocols which have been agreed by the NECN lung group. Because chemotherapy is likely to cause significant toxicity in terms of bone marrow suppression, alopecia, nausea and vomiting and fatigue it should only be administered
by teams which include Oncology Specialists, with the appropriate skills and training.

- The patient should be closely monitored while on treatment and every effort made to address quality of life issues.

- For patients receiving palliative or neoadjuvant chemotherapy, treatment should be discontinued if there is no evidence of a response after 2 cycles or after 1 cycle if there is evidence of progressive disease. Chemotherapy should also be discontinued if the patient has unacceptable toxicity even in the absence of progressive disease.

- Ensure that mechanisms are in place to support the entry of eligible patients into clinical trials, subject to the patient giving fully informed consent. The MDT should record the reasons for patients not being entered into trials that are open.

**Small Cell Lung Cancer (SCLC) Chemotherapy**

- Arrange for patients with SCLC to have an assessment by a thoracic oncologist within 1 week of deciding to recommend treatment.

- Combination chemotherapy has been shown to increase survival and quality of life in patients with SCLC and is superior to single agent therapy even in poor prognosis patients.

**Good Prognosis Patients**

- The prognostic group studies have consistently shown that only the ‘good’ prognosis patients achieve long term survival.

- The recommended treatment in good prognosis patients with limited stage disease, normal haematological and biochemical parameters, good performance status and sufficient respiratory reserve is concurrent chemoradiation with Cisplatin and Etoposide (see chemotherapy protocols for details).

- All other good prognosis patients should be offered a combination of Carboplatin or Cisplatin and Etoposide (see chemotherapy protocols for details). Response should be assessed after 2 cycles and only continued if the tumour is responding. Dose modification may be required in the presence of unacceptable toxicity (See network protocols for guidance). A
total of 4-6 cycles should be given unless there is evidence of progressive
disease or unacceptable toxicity.

- Good performance stage (PS 0,1,2) patients with limited stage disease
who have not undergone concurrent chemoradiation but who achieve a
complete response or good partial response should be offered
consolidative thoracic radiotherapy on completion of their chemotherapy.
- Patients who achieve less than a complete response may be referred for
consideration of palliative radiotherapy if symptomatic.
- Good prognosis patients (limited and extensive disease) who achieve a
partial or complete response to chemotherapy should be referred prior to
their penultimate cycle of treatment for consideration of prophylactic
cranial irradiation (PCI).

**Poor Prognosis Patients**

- Patients should be treated with palliative intent using a combination of
Carboplatin & Etoposide as per the good prognosis patients or a
combination of Vincristine, Doxorubicin and Cyclophosphamide (see
chemotherapy guidelines) in patients not suitable for platinum based
chemotherapy. Response should be assessed after 2 cycles and
chemotherapy only continued if the patient is responding and toxicity is
acceptable. Responding, patients should receive between 4 – 6 cycles of
treatment. The patient should be re-discussed at the multidisciplinary
meeting regarding a referral for radiotherapy following completion of
chemotherapy in the presence of symptomatic disease.

**Clinical trials**

- Ensure that mechanisms are in place to support the entry of eligible
patients into clinical trials, subject to the patient giving fully informed
consent. The MDT should record the reasons for patients not being
entered in to trials that are open.
Disease Relapse

- In patients who relapse more than 3 months following completion of chemotherapy consideration should be given to retreating with their original chemotherapy regime, eg oral Topotecan, providing this is in accordance with patient wishes and their performance status is acceptable. Entry into ongoing clinical trials may be considered if the patient is agreeable. Palliative radiotherapy or symptomatic care however may be in the best interests of the patient.
- If relapse is less than 3 months following treatment these patients fall into a particularly poor category. These patients may be considered for treatment with an alternative chemotherapy regime, for example, oral Topotecan though response rates are likely to be low, or entry into an appropriate clinical trial. Again, palliative radiotherapy or symptomatic care may be more appropriate than further chemotherapy.

Non-Small Cell Carcinoma
Neoadjuvant Chemotherapy

- Neoadjuvant chemotherapy is not routinely recommended in patients with surgically resectable disease, but downstaging neoadjuvant chemotherapy may be considered in patients whose initial staging precludes them from surgery or radical radiotherapy. This must be discussed at the thoracic MDT.

Adjuvant Chemotherapy

- The meta-analysis of 1995 has shown an absolute survival benefit for adjuvant therapy of 5% for Cisplatin based regimes, but the 95% confidence intervals are wide making the actual benefit difficult to assess. Subsequent studies have confirmed a benefit for adjuvant chemotherapy in selected groups of patients. Adjuvant chemotherapy is therefore recommended in patients with stage T1-3, N1-2 M0 NSCLC and T2-3 N0 M0 NSCLC with tumours greater than 4cm in diameter who are of good performance status 0-1, preferably within 8 weeks of surgery. The proposed regimes are Carboplatin and Paclitaxel or Cisplatin and Vinorelbine (see chemotherapy protocols for details).
Combined Chemoradiation

- Consider chemoradiotherapy for patients with stage II or III NSCLC who are not suitable for surgery. Balance potential benefit in survival with the risk of additional toxicities.

- Combining chemotherapy and radiotherapy for patients with stage III disease has been shown to have survival benefits. All patients with good performance status who have stage IIIA disease who are not suitable for surgery and selected IIIB NSCLC patients should be offered combined chemoradiation treatment. Where the patient’s PS, renal function and PFTs allow, concurrent chemoradiation using the SOCCAR regimen should be considered as standard.

- Ensure all patients potentially suitable for multimodality treatment (surgery, radiotherapy and chemotherapy in any combination) are assessed by a thoracic oncologist and a thoracic surgeon.

Palliative chemotherapy

- In patients with stage 3B (not suitable for radical treatment) & 4 disease, chemotherapy may have a role both in symptomatic benefit and possible prolongation of survival. Patients who fit into this category should be fit (PS 0, 1, 2) and be agreeable to treatment. The recommended protocols are a combination of a platinum drug (Cisplatin or Carboplatin) and Pemetrexed for patients with non-squamous histology and for those with squamous cell cancer or non small cell lung cancer not otherwise specified and a 3rd generation drug (Vinorelbine, Gemcitabine, Paclitaxel or Docetaxel) (usually 4 cycles) with single agent Vinorelbine or Gemcitabine reserved for those not suitable for platinum based regimes (see chemotherapy protocols for details). Note patients with non-squamous histology should now be offered Pemetrexed and a Platinum drug.

- In patients with Stage 3B disease who have had a response to chemotherapy it may be appropriate to re-discuss the patient at the multidisciplinary meeting regarding referral for thoracic radiotherapy. Patients with stage 4 disease should be re-discussed at the
multidisciplinary meeting regarding a referral for radiotherapy in the presence of persisting symptomatic disease.

- All patients within this group should be considered for entry into appropriate clinical trials. Current trials include the following:
  - FRAGMATIC

- In patients not suitable for chemotherapy, consideration should be given as to whether they may be suitable for the TOPICAL study, which is looking at the role of Tarceva, an EGFR inhibitor, in the management of patients with advanced NSCLC.

Tyrosine Kinase Inhibitors
(NICE Technology Appraisal Guidance 192, 2010)

- This guidance states that Gefitinib is recommended as a treatment option for the first-line treatment of people with locally advanced or metastatic non-small cell lung cancer (NSCLC) if
  3. They test positive for epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation and
  4. The manufacturer provides gefitinib at the fixed price agreed under the patient access scheme. Gefitinib is given as an oral 250mg tablet daily, and is being supplied by the manufacturer at a fixed price under a patient access scheme. Under this scheme there is a fixed cost of £12200 per patient once the third pack is provided, so assessment of response to treatment before the end of the 2nd month is essential.”

- The NECN Lung NSSG recommends that this guidance is followed. Current policy which is regularly reviewed (July 2011) is to request EGFR mutation testing on all suitable patients following MDT discussion. In addition EGFR mutation testing can be requested before MDT discussion at the discretion of the treating clinicians if it is highly likely that this treatment might be a possibility. EGFR mutation testing can also be requested at any later stage if the clinicians feel that this would be clinically beneficial to the patient. Second Line Chemotherapy and TKIs

- In good performance status patients who have had a durable response (more than 6 months) to first line chemotherapy it may be appropriate to
consider retreatment with the original regime. The alternative recommendation is consideration of single agent Docetaxel as per the NICE guidelines. Again all patients should be considered for entry into appropriate clinical trials.

- Patients may be offered erlotinib (Tarceva) as an alternative to docetaxel. This decision will be at the discretion of the oncologist and will take into account patient preference. In patients will BAC, erlotinib should be considered the drug of choice.
# APPENDIX ONE: NECN APPROVED LIST OF REGIMENS FOR LUNG

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