PRINCESS MARGARET CANCER CENTRE
CLINICAL PRACTICE GUIDELINES

LUNG SITE

LUNG CANCER

Lung Site Group – Lung Cancer

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1. INTRODUCTION

Lung cancer is the most common invasive malignancy in the world and the most common cause of cancer deaths in Western countries. In North America, it accounts for more deaths than the next three most common cancers (breast, prostate and colon) combined. Despite a reduction in smoking rates, tobacco remains the major etiological factor in lung cancer development. Lung cancer is divided into two major subgroups; non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). The most common pathologic subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma. NSCLC is potentially curable with surgical resection in its early stages, however most patients present with locally advanced or metastatic (incurable) disease.

Small cell lung cancer (SCLC) currently accounts for approximately 15% of all cases of lung cancer and its incidence is declining. SCLC is an aggressive thoracic malignancy with a propensity for early spread to distant sites, particularly the brain. SCLC is traditionally categorized into limited or extensive stage however now should be staged according to the joint UICC & AJCC Staging Seventh Edition, 2010.

2. PREVENTION

The most effective prevention strategy for lung cancer is tobacco product avoidance, with avoidance of smoking or smoking cessation. All agreeable individuals should be referred for smoking cessation programs. Other possible strategies to prevent lung cancer include reducing occupational exposure to smoke and other carcinogenic substances and reducing residential and occupational radon exposure. However, at least 15% of lung cancer patients are not related to smoking, and with changing population demographics with increasing immigrants from East Asia, this rate is increasing.

3. SCREENING AND EARLY DETECTION

Traditionally, there was not proven screening method for early detection of lung cancer. Neither routine chest X-ray (CXR) nor sputum cytology had been proven useful. Several studies have explored the potential usefulness of low-dose Computed Tomography (LDCT) scans for screening of high risk current and former smokers. Single arm studies reported 10-year survival rates of up to 92%. The largest randomized controlled study, the National Lung Screening Trial (NEJM. 2011 Aug 4;365(5):395-409), has demonstrated a significant reduction (20%) in lung-cancer specific mortality; this study enrolled more than 50,000 current and former smokers (>30 pack-year, quit < 15 years) in the age between 55 to 74.

As this study has only recently been reported and has major logistics and financial implications related to a systematic adoption of this screening program, it has not become

available in most jurisdictions, including Ontario. Currently CT screening for lung cancer is available in Canada only in the context of a few research protocols.

4.   **DIAGNOSIS**

At the time of the initial assessment, patients (particularly those with potentially curable cancers requiring multimodality input and/or treatment) should be assessed in a multidisciplinary environment.

Clinical Evaluation:
- Complete history and physical examination in all patients
- History of pain, shortness of breath, cough, hemoptysis, stridor, hoarse voice, dysphagia
- Duration and extent of weight loss, if any
- Performance status (WHO/ECOG or Karnofsky)
- Co-morbid conditions (previous cancers, COPD, heart disease, cerebrovascular disease, TB, hepatitis, renal dysfunction, hearing loss or neuropathy)
- Quantitative documentation of tobacco and alcohol use, occupational carcinogen exposure
- Social & personal history (secondary exposure to smoke, asbestos)
- Prior exposure to irradiation, if any
- Prior treatment of cancer, if any
- Inspection for signs of dyspnea, anemia, cyanosis, clubbing, jaundice or edema
- Palpation and auscultation of the chest
- Palpation of the neck and supraclavicular regions for palpable lymph nodes
- Abdominal assessment for organomegaly
- Baseline body weight should be measured in kilograms and height in cm, with a calculation of body surface area

Oncologic Imaging and Laboratory Evaluations:
Evaluation of the Intrathoracic extent of disease:
   A chest xray is of limited use in lung cancer imaging although it is clinically useful to have as a baseline, to compare to follow-up CXR and assess for acute changes. To assess the full extent of the tumor and lymph node involvement, a contrast-enhanced CT of the chest is required. A Magnetic Resonance Imaging (MRI) of the chest is indicated in selected cases only, primarily to assess potential invasion of the tumor into neighboring structures and organs (e.g. brachial plexus, thoracic spine, heart or mediastinal vessels).

Metastatic Workup
   Imaging to determine presence or absence of metastases includes the following:
- A contrast-enhanced CT of the abdomen to detect metastases in liver and adrenals. Further tests, such as an ultrasound, MRI adrenals or liver or a special

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dedicated adrenal CT may be needed if abnormalities are found that need further characterization
- A contrast-enhanced MRI of the brain is the most sensitive method to detect cerebral metastases and is the study of choice in our institution. If MRI is unavailable a CT of the brain should be performed.
- A nuclear medicine bone scan detects metastases in the skeleton (which may also be seen on PET CT, and thus this test is not always employed)
- FDG-Positron emission tomography (PET) -CT is the staging method of choice for potentially resectable Stage I - III NSCLC and limited stage SCLC. Compared to the conventional staging methods mentioned above, it has been shown to demonstrate additional tumor sites in lymph nodes (N stage) and distant locations (M stage), yielding potential upstaging and change in management. However, false positive and false negative rate needs to be considered and further tests (eg biopsies) may be required.

Laboratory Tests:
- Baseline CBC, electrolytes, calcium, albumin, creatinine, liver function studies, LDH

Other Investigations:
- Bronchoscopy, biopsy of endobronchial lesions, brushings and washings
- CT-guided trans-thoracic fine needle aspiration or core biopsy for lesions not diagnosed by bronchoscopy
- Mediastinal lymph node sampling (EBUS, mediastinoscopy) to stage mediastinal lymph nodes in patients being considered for loco-regional treatment
- Excisional biopsy or needle biopsy of readily accessible secondary deposits (eg supraclavicular nodes, liver metastases) if relevant to diagnosis or staging
- Pulmonary function tests should be performed , in patients being considered for radical treatment.

5. **PATHOLOGY**

All patients should have documentation of the tumour histology and its subtype (See WHO Classification for lung cancer below). On rare occasions where urgent palliation is required and the biopsy is not feasible or will delay care, the clinical and radiological diagnosis of lung cancer may be sufficient to proceed with management. Pathology reports in lung cancer should specify histological subtypes and patterns of the tumor, as best as they could be defined morphologically or by recognized immunohistochemical markers. In resection specimens, reports on type of specimen, location of tumor, tumor size, lymph node status and bronchial resection margins status must also be provided, so that an accurate pathological staging of the tumor can be rendered.

• Institutional pathology review for patients whose tumor diagnoses were made at outside institutions are conducted at the request of treating oncologists. There is a multi-disciplinary agreement that institutional pathology review for external

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diagnoses of small cell carcinoma, large cell carcinoma, poorly differentiated carcinoma, mesothelioma and thymoma is useful and should be obtained

• Fine needle aspiration biopsy of suspected metastatic disease may be performed in selected cases.

• Open surgical biopsy of metastatic disease is not indicated unless there is doubt about the diagnosis, or therapy dictates that histopathological subtyping or molecular studies are required, or when no index primary has been documented.

•Cytological assessment of pleural/pericardial fluid if appropriate.

Biomarker testing of samples has become important both in treatment selection and prognostication. A project is underway at UHN, routinely profiling new lung cancer specimens using the Oncocarta v.1, using the MassARRAY technique (Sequenom).This includes testing for activating EGFR mutations (in adenocarcinoma), and a panel of 238 potential mutations in 19 oncogenes including KRAS, BRAF and PIK3CA. EGFR mutation status is currently used for initial treatment selection in advanced NSCLC patients where appropriate.

While currently the 2004 WHO classification is the official classification system that are used for diagnosis, a revised IASLC/ATS/ERS classification for adenocarcinoma (*J Thorac Oncol.* 2011;6: 244–285) has been published. The adoption and implementation of this classification system remains as an addendum to the WHO classification. Both are provided in Appendix I.

Staging of both NSCLC and SCLC is according to the Joint UICC & AJCC Staging Seventh Edition, 2010, the details of which are supplied in Appendix II. The following is a brief summary of the clinically relevant stages of lung cancer:

- Stage I = early lung lesion, no lymph node involvement (T1T2aN0M0)
- Stage II = more advanced lung lesion with no lymph nodes (T2bT3N0) or earlier lesion with first eschalon nodal involvement (T1T2aN1M0)
- Stage III = any tumor with mediastinal nodal involvement (T1-4N2-3), or a very locally advanced tumor without mediastinal involvement (T3T4N1, T4N0M0)
- Stage IV = distant metastases (pleural or beyond)

6.   **MANAGEMENT**

6.1 Non-Small cell Lung Cancer (NSCLC)

6.1.1 EARLY STAGE NSCLC – STAGE I-II:

All patients are considered for potential cure. Surgery is the usual consideration if a patient is medically operable. Depending on findings at surgery, patients may require adjuvant chemotherapy. Radiotherapy is a consideration for patients who are considered either high risk for surgery, or who are medically inoperable, or who refuse surgery. Conventionally fractionated radiotherapy has traditionally given much poorer local control and survival than surgery. Advances in RT techniques, namely stereotactic body radiotherapy (SBRT) have led to use of this option for a larger number of patients, due to its non-invasive nature, low risk of acute toxicity and high reported rates of local control. However, depending on the location of the tumor, complications and toxicities may arise. As well, without a surgical intervention, there is a risk of under-staging, by not detecting occult nodal metastases, especially in N1 nodes. Suitable patients should undergo mediastinal staging with EBUS or mediastinascopy. Moreover, the true rates of long-term local control after SBRT are still not known. Thus, SBRT is not at this time considered as a comparable treatment option to surgery, especially not in patients who are medically fit to undergo surgery.

Surgery
The optimal treatment for early stage lung cancer is surgical resection. Patients are staged with CT and PET scan. Preoperative pathological sampling of mediastinum (through mediastinoscopy or endobronchial ultrasound (EBUS) guided fine needle aspiration) is advisable for all except those patients whose primary is less than 2cm and located in the peripheral 1/3 of the lung. Usual surgical approaches for early stage lung cancer include video-assisted thoracotomy (VATS) or an open thoracotomy. Lobectomy is currently the preferred treatment for stage I/II lung cancer. In patients with limited lung function a segmental resection or a wedge resection may be performed. The role of sub-lobar resection (segmental or wedge) in patients' with stage I/II lung cancer with adequate lung function is currently the subject of several clinical trials.

Lymph nodes and the bronchial resection margin should be assessed by frozen section during surgery should there be concerns about involvement. Some patients have findings during surgery which preclude resection such as unanticipated N2/3 disease, pleural metastasis or invasion of critical organs.

At the time of surgery a thorough mediastinal lymph node assessment must be performed. The lymph nodes should be reported in the pathology report according to the IASLC/UICC staging diagram.

Chemotherapy
Patients with resected stage II (N1) NSCLC benefit from adjuvant chemotherapy as demonstrated in several randomized controlled trials and the LACE Meta-analysis. Patients with stage I lung cancer ≥4cm in size may also benefit from adjuvant chemotherapy. All patients meeting these criteria should be referred to medical oncology for a discussion of the pros and cons of adjuvant chemotherapy. Patients who are very elderly, have poor performance status (PS) or multiple co-morbidities may not be candidates for adjuvant chemotherapy. The recommended regimen is four cycles of cisplatin and vinorelbine (see Appendix III 1.). Patients not suitable for cisplatin may receive carboplatin. Chemotherapy should commence 6-8 weeks post surgery as long as patient has recovered sufficiently post surgery without evidence of active infection.

Radiation Therapy
For patients who are not candidates for surgery and have an early stage T1T2N0M0 NSCLC, SBRT, hypofractionated or conventional RT are a consideration. SBRT is preferred, unless the risks of high dose per fraction RT are considered too high for the given tumor and/or patient – usually that is due to size of tumor, proximity to critical structures or previous high dose RT, or other patient factors.

Stereotactic body radiotherapy (SBRT)
SBRT may be considered for NSCLC (T1, N0, M0; T2 (≤ 5cm), N0, M0; or rarely T3(≤ 5cm), N0, M0 chest wall primary tumors. The dose of SBRT depends on the lesion size and location.

- 54Gy in 3 fractions for peripheral tumors, away from organs at risk (OAR)
- 48 Gy in 4 fractions for peripheral tumors <3cm in diameter, close to ribs or other OAR
- 60 Gy in 8 fractions for centrally located tumors (i.e tumors within a 2 cm radius of the airway, great vessels and other mediastinal structures)

The 3 or 4 fraction schedules are given every 2-4 days apart; a minimum of 48 hours between treatment and maximum overall treatment time of 14 days. The 8-fraction schedule is given daily.

Hypofractionated RT
For patients with early stage lung cancer not suitable for SBRT, a somewhat hypofractionated regiment is considered, typically 60Gy in 20 fractions or 50Gy in 20 fractions.

Conventional RT
For patients with early stage lung cancer not suitable for SBRT or hypofractionated regimens, conventional regimens include 60Gy in 30 fractions, 66Gy in 33 fractions and 70Gy in 35 fractions. They have the advantage of conventional dose per fraction, with potentially less late normal tissue injury, but a lesser biological dose.

Post Operative Radiotherapy

Rarely, post-operative radiotherapy is a consideration in early stage lung cancer, if the margins are close or positive and re-resection is not felt to be advisable. The case should be discussed with the surgeon to identify the area of concern. At present, 54Gy in 27 fractions for close margins and 60Gy in 30 fractions for positive margins. The timing of PORT and adjuvant chemotherapy is considered on a case-by-case basis, weighing the concerns about risk of local recurrence versus the risk of systemic disease progression. PORT is generally given after chemotherapy for close margins and possibly before chemotherapy for positive margins.

Patients with gross residual disease after surgical resection should be discussed in a multidisciplinary setting and therapy individualized.

There is no role for mediastinal RT in completely resected N0 or N1 disease, as confirmed by survival detriment seen in this group of patients in the PORT meta-analysis.

6.1.2 Locally Advanced NSCLC (stages IIIA and IIIB):

Stage IIIA
Patients with stage IIIA NSCLC are a heterogenous group. The majority of IIIA patients have N2 disease, but with varying amount and extent of disease:

- resected tumors with microscopic metastases to lymph nodes found at time of surgery
- resectable tumors with microscopic LN involvement found at preoperative assessment
- single station grossly involved mediastinal LN
- multi-station ipsilateral LN
- unresectable bulky nodal stations

In addition, T3N1,T4N0 and T4N1 are also part of stage IIIA.
The decision regarding appropriate treatment focuses on two questions :
1. Is the goal for this patient curative or palliative?
2. If curative, is bimodality or trimodality therapy more appropriate?

Curative Goal
Patients with stage IIIA should be considered for curative treatment as long as their life expectancy, PS, comorbidity and age do not preclude it. In particular, patients with stage IIIA due to T3N1,T4N0/N1 benefit from aggressive treatment in order to provide better chances of local control (in view of lesser risk of distant progression given absence of mediastinal LN involvement). Patients with poor PS (2 or worse), presence of poor prognostic factors (weight loss, hypercalcemia, thrombosis, etc), very significant comorbidity and very advanced age may not tolerate aggressive treatment and may not benefit. Some of these factors may affect the administration of one of the treatments but not others. In selected situations, if chemotherapy is contraindicated, radical radiotherapy

alone may be a consideration for curative treatment, particularly for very elderly patients with good PS, patients whose comorbidities preclude chemotherapy but whose extent of disease is encompassable by high dose RT field.

Bimodality vs Trimodality treatment
For patients considered for curative intent, decision needs to be made up front re bi-modality vs trimodality therapy. These decisions depend on the sub-stage of IIIA, precise tumor location, tumor bulk as well as patient factors.

If N2 disease is found after surgical resection, patient should receive post- operative chemotherapy (in view of survival benefit). The role of postoperative RT (PORT) in N2 disease is controversial. Data from RCTs demonstrated a local control benefit; the PORT meta-analysis did not report a survival detriment in N2 patients. In a retrospective subgroup analysis of the ANITA trial, postoperative N2 patients who were selected to have PORT and randomized to chemotherapy arm had improved survival; however, these data are hypothesis generating only. We consider PORT for selected patients where there is a particular concern about regional control and who are medically fit, with expectations of low toxicity from RT. PORT is generally given sequentially after chemotherapy in this circumstance given the survival benefit conferred by adjuvant chemotherapy. The only situation in which concurrent postoperative chemoradiotherapy would be considered is in the case of gross residual disease. This is usually employed only in very fit patients because, while there is no detriment to survival from the concurrent approach, acute toxicities can be more pronounced.

If N2 disease is known preoperatively and considered resectable, eg single station, non bulky N2, or occasionally very fit patients with multistation non-bulky N2 disease, those patients will be considered for neo-adjuvant chemo-radiotherapy followed by restaging approximately 4 weeks after, followed by surgery if no evidence of progression and patient well enough for surgery. Following surgery, patient is reassessed for consolidation chemotherapy. In rare situations, neoadjuvant chemotherapy alone, without RT, is recommended - either because RT may not be possible (eg previous RT in the area, idiopathic pulmonary fibrosis or other contraindications) or there is concern about its impact on an anticipated challenging surgical procedure (eg sleeve lobectomy). Two to four cycles of vinorelbine/cisplatin or similar doublet may be considered (Appendix III 1 or 3a.). RT may be considered postoperatively in the latter setting, if margins are a concern.

If N2 disease is not resectable, due to bulky single station or multi station N2 disease those patients should be considered for primary concurrent chemoradiotherapy. Some of those patients may later be reassessed for surgery.

Patients who are deemed to require a pneumonectomy are considered higher risk in terms of morbidity and mortality following chemoRT surgery, but in well selected and well informed patients, that may still be the preferred treatment approach.

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Many of the patients with IIIA tumors that do not have mediastinal LN involvement will be potentially resectable. This includes T3 tumors invading chest wall, apical tumours or focal pericardial or phrenic nerve invasion as well as T4 lesions with requiring complex surgery and reconstruction eg of the carina, vertebral body, or -separate tumour nodules in a different ipsilateral lobe with pnemonectomy.

For resectable T4N0/N1 or Superior Sulcus/Pancoast (T3/4,N1) tumors, standard therapy is neoadjuvant chemoradiotherapy followed by surgery. For resectable T3/4,N1 tumors , either surgery up front followed by adjuvant chemotherapy +/- PORT if positive margins, or neoadjuvant ChemoRT followed by surgery are the main considerations. Patients with unresectable T4,N0/N1 T3N1 are considered for chemoradiotherapy. Selected patients may later be reassessed for surgery after completion of definitive chemoRT.

Palliative Goal
For patients with:
- Poor PS (ECOG 3 or 4)
- Significant co-morbidities that preclude delivery of chemoRT
- Very advanced age that may make chemoRT difficult to tolerate
- Very extensive loco-regional volume of tumor that makes radical RT too toxic

These patients will not tolerate combined modality curative treatment. Treatment options include:
1. Radical radiotherapy alone – may be with palliative or curative expectations
2. Palliative radiotherapy
3. Chemotherapy alone
4. Supportive care

The most common treatment recommended for the scenarios listed above are:
- Poor performance status (ECOG 3 or 4)-- palliative RT if they have symptoms or impending symptoms
- Significant co-morbidities that preclude delivery of chemoRT -- radical or palliative RT depending on the tumor location and the perceived risk/benefit of RT
- Very advanced age that may make chemoRT difficult to tolerate -- radical or palliative RT depending on the tumor location and the perceived risk/benefit of RT
- Very extensive loco-regional volume of tumor that makes radical RT too toxic -- consideration of chemotherapy if good PS, or palliative RT if symptoms
- Inability to accurately define extent of thoracic disease -- consideration of chemotherapy if good PS, or palliative RT if symptoms

However, these treatment discussions need to be individualized and should take into account patient factors including their understanding, values and preferences. A thorough discussion in a multidisciplinary setting is highly desirable.

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Stage IIIB (T1-T4N3 or T4N2M0)

Patients with Stage IIIB disease are for the most part not resectable, with the possible exception of well selected and very fit patients with T4N2 tumors. For most patients, the decision regarding appropriate treatment focuses on two questions:

1. Is the goal for this patient curative or not?
2. If curative, is concurrent chemoRT appropriate?

The vast majority of these patients are N3 and need to be assessed in terms of their fitness to undergo curative treatment. They should be considered for curative treatment as long as they do not have significant co-morbidities, poor PS and/or poor life expectancy that would preclude radical treatment, and as long as the disease is amenable to radical radiation.

Curative Goal

Our standard bimodality treatment is concurrent platinum-based chemotherapy and high dose thoracic RT for patients who are medically fit for combined concurrent chemotherapy and whose tumor is encompassable within a tolerable RT volume respecting organs at risk.

If the tumour bulk is too large to allow tolerable radiation volume, patient may have (neoadjuvant) chemotherapy followed by a reassessment and radical radiotherapy or concurrent chemoRT if the tumour shrinks sufficiently

Some patients who may not be fit enough for concurrent chemoRT or are quite elderly may be considered for sequential chemo RT - either radical RT first, followed by adjuvant chemotherapy, or occasionally a trial of chemotherapy, followed by radical RT. These decisions need to be personalized to the patient's clinical situation and need to be made in a multidisciplinary setting and with involvement of the relevant specialties.

Radical RT alone is a consideration for patients who are not chemotherapy candidates, due to their comorbidity or very advanced age. For patients who are of good PS and with no other adverse features, this may be considered to be of curative intent.

Palliative Goal

Stage IIIB patients with unfavourable features (extensive and/or bulky disease, poor PS, significant weight loss) may not be fit for radical treatment, and are treated with palliative intent.

Treatment options for these patients include:
1. Radical radiotherapy (this may occasionally result in prolonged survival although whether or not it offers a cure depends on prognostic factors)
2. Palliative radiotherapy (if thoracic disease is causing symptoms, or expected to cause symptoms, or if patient is not a candidate for chemotherapy and RT is considered to be worthwhile)
3. Palliative chemotherapy (if patient is fit enough for chemotherapy)
4. Best Supportive care

Surgery
Surgery for stage III NSCLC is either done because of lack of evidence for mediastinal LN involvement (ie preoperative assessment of LN didn't reveal involvement) or in the setting of planned tri-modality treatment (typically neoadjuvant chemoRT followed by surgery, occasionally surgical resection followed by adjuvant chemo and/or RT if there are particular concerns about the effect of neoadjuvant treatment on the surgical outcomes, especially morbidity). Given that standard approach is a thorough pre-operative assessment, and that mediastinal nodal involvement, when identified surgically, can still be amenable to resection, in most cases the resection will be completed, preferably an R0 resection (no residual tumor). Debulking procedures do not constitute appropriate oncological management. In rare situations, when toxicity of radiation to large primary tumors may impact on the ability to deliver chemoRT, it may be appropriate to resect the primary tumor even if the mediastinal nodal disease is not resectable, as chemoRT can provide local control within the mediastinum. Such situations are best discussed in a multidisciplinary setting prior to embarking on treatment.

Depending on the location of the tumour, surgery may include lobectomy, bilobectomy or occassionally pneumonectomy (eg if the tumor is very proximal or involves the hilum). A sleeve lobectomy will avoid a pneumonectomy in patients with tumor extension into a main bronchus or the trachea. Typical approach is a lateral thoracotomy approach. VATS is used for patients who are not thought to have mediastinal nodal involvement.

Lymph nodes and the bronchial resection margin should be assessed by frozen section during surgery should there be concerns about involvement. However, surgery will proceed even if the lymph nodes continue to demonstrate cancer after induction treatment. At the time of surgery a thorough mediastinal lymph node dissection must be performed. The lymph nodes should be reported in the pathology report according to the IASLC/UICC staging diagram.

T4 tumors involving vertebral body are resected through a two stage combined thoracic surgery/orthopaedics approach with the initial surgical procedure involving the mobilization of the involved part of the spine and/or chest wall and fixation of the spine with rods, followed typically within a week with an en-bloc resection of the lung tumor and the spinal/chest wall tumor, done jointly by the two surgical specialties. This two stage procedure allows for easier postoperative recovery and fewer complications, and is considerably shorter than the 16+ hrs that would be needed to perform this in one sitting.

Superior Sulcus or Pancoast tumours may require an anterior approach to the resection. If the tumor is known to have significant brachial plexus involvement, a neurosurgeon specializing in brachial plexus surgery may be called to perform that part of the resection.

For stage IIIB tumors, surgical management is not usually a primary treatment approach, with a possible exception of well selected patients with T4N2 NSCLC.

Chemotherapy
Patients need to be assessed for the ability to tolerate systemic therapy. Considerations include performance status, co-morbidities (e.g. cardiac failure, renal or hepatic impairment, underlying chronic hepatitis, hearing problems or neuropathy, bleeding diatheses, bone marrow reserve), and the ability to consent and understand the risks. Patients also require sufficient social support to tolerate treatment and the ability to seek emergency care for potentially life-threatening toxicity, such as neutropenic sepsis. Dose reductions may be considered, depending on PS or renal or hepatic impairment, or prophylactic antibiotics in the setting of obstructive pneumonia. Cisplatin is generally favoured in a curative or adjuvant setting. Carboplatin may be substituted for cisplatin in patients with renal impairment, ototoxicity, peripheral neuropathy or where additional hydration is contraindicated.

Adjuvant chemotherapy post resection for IIIA (for patients who had no preoperative chemotherapy):
4 cycles of Cisplatin and vinorelbine (Carboplatin if cisplatin contraindicated), as outlined in Appendix III 1. Chemotherapy should commence 6-8 weeks post surgery as long as patient has recovered post surgery without evidence of active infection.

Chemotherapy as part of trimodality approach for Stage IIIA:
2 cycles of concurrent chemoRT prior to surgery are used, commencing on day 1 of radiation. The SWOG protocol is used, and outlined in Appendix III 2a, with etoposide administered days 1 through 5, and cisplatin on days 1 and 8 every 28 days during radiation.

Consolidation chemotherapy following surgical resection, when patients have sufficiently recovered, will be considered for fit patients, especially if induction treatment led to a tumor response. The SWOG protocol (etoposide days 1 through 5/cisplatin days 1 and 8) may be used again for an additional 2 cycles, or as an alternative, a standard 21-day platinum doublet regimen, most commonly vinorelbine/cisplatin, may be used (detailed in Appendix III 2b). Two cycles of consolidation therapy are given, for a total of 4 cycles including those delivered concurrently.

Neoadjuvant chemotherapy with a platinum doublet, most commonly vinorelbine/cisplatin (Appendix III 1 or 3a) may be offered for 2 to 4 cycles in selected IIIA patients who are planned for surgery, and in whom RT is contraindicated or preopRT is not planned.

Concurrent chemoRT for "bimodality" stage IIIA and IIIB patients (no planned surgery)
The SWOG protocol, outlined in Appendix III 2a is used concurrent with chemoRT. Consolidation platinum-based chemotherapy is often recommended for patients who are tolerating treatment, maintaining their PS and progression-free. The SWOG protocol (etoposide/cisplatin) may be used, or as an alternate, the 21-day vinorelbine/cisplatin combination for an additional 2 cycles (Appendix III 2b). Consolidation treatment would not be given to patients whose PS or comorbidities have worsened after concurrent chemoradiation.

Radiation Therapy

Radiation as part of Trimodality Treatment (Neoadjuvant Concurrent ChemoRT followed by surgery):

Thoracic RT with 6-10 MV photons on Linear Accelerator, 45Gy/25 fractions/5weeks (1.8Gy per fraction) Monday to Friday, with concurrent chemotherapy starting on day 1 of RT as described above (usually the start day is Monday to maintain 5 sequential days of Etoposide although it may start on Tuesday as well).

Primary tumor and known nodal disease as well as the draining hilum and neighboring nodal stations are included in the target volume, with margin for tumor motion (as determined by 4D planning CT) and setup variations. Either 3D conformal or IMRT (intensity modulated) RT is utilized. Image guidance is performed daily using cone beam CT or other volumetric imaging, with verification of position using spine and carina as surrogate structures. Patients are seen weekly in review for assessment of toxicity.

Surgery is performed 4-6 weeks after completion of treatment, provided that there is no evidence of progression and that the patient is well enough for surgery. In most cases, surgery is complete and no adjuvant RT is needed. However, if the patient is not a surgical candidate after the neoadjuvant treatment, or if they are taken to surgery but tumor has not been resected, a further dose of 20Gy is considered, with concurrent chemotherapy. It is preferable to administer it as soon as possible as a break between the first and the second course of RT diminishes its biological effectiveness. If a patient has progression of disease during or after completion of neoadjuvant chemoRT, completion of a radical dose of RT is rarely indicated, although it could be considered on a case-by-case basis.

Radiation as part of Bimodality Treatment (Concurrent chemoRT)

Thoracic RT with 6-10 MV photons on Linear Accelerator 66 Gy/ 33 fractions/ 6.5 weeks (2Gy per fraction) with concurrent chemotherapy starting on day 1. The primary tumor and known nodal disease are included in the target volume, with margin for tumor motion (as determined by 4D planning CT) and setup variations. Consideration is given to uncertainties of disease extent, especially in terms of nodal volume. PET and IV contrast may be helpful in that regard to delineate extent of disease. Most plans are done with the benefit of IMRT. Image guidance is performed daily using cone beam CT or other volumetric imaging, with verification of position using spine and carina as surrogate structures. Patients are seen weekly in review for assessment of toxicity.

Radical Radiotherapy alone:

If chemotherapy is not employed, and patient is treated for stage IIIA or IIIB disease with radical RT alone, typical doses are 66-70 Gy/30-35 fractions/6.5-7weeks. Occassionally, 50Gy/20 fr or 60 Gy/20 fr are considered, if shortening the overall time is desirable, and if an increase in fraction size is not deemed to be associated with high risk of normal tissue toxicity. Principles of planning and treatment are the same as outlined above.

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Endobronchial Brachytherapy (High dose rate (HDR) brachytherapy)**:**
At times, this is used as adjunctive "boost" therapy for endobronchial tumors, following a course of external beam RT, eg 45 Gy/25 fr followed by 2 x 8 Gy endobronchial RT (1 week apart) with HDR endobronchial application of iridium, prescribed to 1cm from the source for invasive tumors with an endobronchial component

Even less often, endobronchial RT can be considered for primary irradiation of small non-invasive mucosal tumours of the proximal bronchus or trachea, eg 7 Gy x 6 applications 1 week apart.

Postoperative Radiation
The role of PORT in N2 disease is controversial. We consider PORT for selected patients where there is a particular concern about regional control and who are medically fit, with expectations of low toxicity from RT. The volume of PORT should be individualized based on the tumor location and the location(s) of positive LN although it may include the entire mediastinum. The typical dose for a R0 resection is 54Gy in 27-30 fractions (at 2 or 1.8Gy/fr respectively). PORT is generally given sequentially after chemotherapy in this circumstance given the survival benefit conferred by adjuvant chemotherapy.

Patients with gross residual disease after surgical resection should be discussed in a MDT and therapy individualized. The only situation in which concurrent postoperative chemoradiotherapy would be considered is in the case of gross residual disease. This is usually employed only in very fit patients because, while there is no detriment to survival from the concurrent approach, acute toxicities can be more pronounced.

Palliative radiotherapy
Choice of palliative dose depends on the PS, extent of intra and extra thoracic disease, estimated life expectancy, symptoms needing palliation, volume that needs to be covered and the estimated toxicity, availability of other treatments (eg plans to proceed w chemotherapy) and patient preference.

Commonly utilized fractionations include 8-10 Gy single fraction, 20 Gy/5 fr, 30 Gy/10 fr and 36-39 Gy/12-13 fr:
- Single fraction (or rarely 17 Gy/2 fr) is utilized for very unwell patients with significant symptoms (eg hemoptysis, airway compromise) and limited life expectancy
- 20 Gy/5 fr is the most commonly prescribed fractionation schedule as it is well tolerated and has a palliative benefit; it however requires daily visits and its benefit takes a bit longer to manifest itself than the single fraction regimen
- 30Gy/10fr is considered in patients with good PS where a better local control is desired; it is however associated with greater esophagits and a risk of pneumonitis
- The more prolonged fractionations of 36Gy/12 fr or 39Gy/13 fr (that needs to be delivered in part with an off-cord technique) tend to be reserved for patients with good PS and no or minimal disease outside the lung, who are likely to have a longer life expectancy

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- Rarely, 50 Gy/20 fr is considered in selected situations where local control is deemed very important ("radical palliation")

Only the symptomatic and/or imminently symptomatic disease needs to be included in a RT field for palliative RT to be of benefit. APPA technique, with shielding, is typically employed, although lung and cord sparing techniques may be of benefit in selected situations. Technological advances, such as 4DCT, IMRT and IGRT may be of benefit in selected situations.

Radiation Therapy Simulation and Planning (pertains particularly to radical RT):

All patients being planned for radical RT should receive 4DCT simulation.   IV contrast may be used for more precise delineation of tumor, especially hilar and mediastinal lymph nodes. All patients must have written consent prior to simulation. Patients are immobilized supine on a chest board with both arms above their head supported by arm cradles. Patients with pancoast (apical) tumors or supraclavicular lymph node involvement are immobilized in a S-frame mask with arms at their sides to ensure reproducible setup of the spine and brachial plexus.

A CT scan is obtained from 5cm above the apex to 5cm below the most inferior part of the lung. A helical scan is done in case 4DCT has too many artifacts that prevent the 4D scan from being used for planning. If contrast is requested, it should be administered immediately prior to helical scan in order to ensure correct timing for image acquisition with respect to contrast washout.

On the inhale and exhale scans, gross tumor volume (GTV - indicating known tumor, primary and nodal), clinical target volume (CTV - indicating potential areas of microscopic disease, eg due to contouring uncertainty, lack of diagnostic information or routes of spread of cancer) will be delineated then combined to form an internal target volume (ITV) and then expanded into a planning target volume (PTV - that accounts for intrafraction and inter fraction motion and uncertainty of setup). The typical CTV expansion is 5mm although this is subject to clinical judgment and is case-specific, and the typical PTV expansion is 5mm on the basis of our setup accuracy data; at times this may be reduced to 3mm. The organs at risk (OARs), namely lungs, esophagus, spinal canal, heart and if need be, brachial plexus, vessels, liver, stomach and other organs, will be contoured on the exhale dataset. Dose volume histograms for all targets and OARs will be carefully reviewed prior to approving the plan, to ensure the optimal therapeutic ration (risk/benefit) of the proposed plan. RT dose may have to be lowered if the plan cannot achieve standard safety criteria. Alternatively, if in a particular case, it is necessary to accept higher risks to an OAR in order to provide a chance for tumor control (eg in the case of an unresectable or marginally resectable T4N0 cancer causing vertebral body invasion including disease in the spinal canal), the specific risks and rationale behind proceeding with an RT plan that exceeds the usually accepted normal tissue toxicities needs to be discussed with the patient and documented accordingly. All plans

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will have physics QA and should have contours and the plan reviewed in lung QA rounds prior to or at the latest within the first week of treatment.

6.1.3. <u>Metastatic Disease (Stage IV</u>)

Metastatic NSCLC represents an incurable situation in virtually all cases. Exceptions to that are some patients with solitary brain metastases, who may be long-term survivors and apparently cured with an aggressive approach to both their thoracic and cerebral tumors (in the case of synchronous metastasis, i.e. discovered at the time of presentation), or those patients who develop a solitary brain metastasis after control of their lung cancer (metachronous metastasis). If a patient has more than one brain metastasis, or solitary extracranial metastasis, they may be long term survivors but it is not likely that they will be indeed cured with aggressive treatment. Other exceptions include solitary adrenal metastasis, which may also potentially be resected for long term disease-free survival or cure, and patients with a contralateral lung lesion as the only evidence of M1 disease, as this may be a synchronous primary T1N0 cancer, pathologically different from the index lesion. In these scenarios, it is worth considering an aggressive approach to both lesions, and multidisciplinary discussion may facilitate treatment recommendations.

For the majority of patients with Stage IV NSCLC, whether at initial diagnosis or with metastases diagnosed at a later date, the goals of care are palliation of symptoms, improving or maintaining quality of life (QOL), and prolonging survival. Prognosis of patients with stage IV NSCLC is limited, especially in the presence of symptomatic brain metastases and/or poor PS (median survival 3 months). Patients with good PS have median overall survival of 8 to 12 months. Patients with detectable driver mutations in their tumours (e.g. EGFR activating mutations, ALK fusions) have usually longer overall survival, especially when treated with targeted agents like EGFR tyrosine kinase inhibitors (TKIs) or anti-ALK agents like crizotinib despite the fact that they usually present with more extensive and advanced disease.

The mainstay of treatment options for stage IV NSCLC are systemic therapy and supportive care. Palliative radiotherapy is commonly employed for rapid symptom relief, and palliative surgery in selected situations, usually after multidisciplinary discussion. All patients with stage IV NSCLC should be referred to palliative care as early as possible, based on recent evidence that quality of life and psychosocial outcomes are improved, as well as the potential for significant additional survival benefit.

Stage IV Treatment options include the following:
- systemic therapy (chemotherapy or targeted therapy) for good PS patients
- supportive care
- palliative radiation to the chest or symptomatic areas of metastases
- palliative surgical procedure

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Chemotherapy
Palliative systemic therapy will be considered for patients with PS.
Chemotherapy prolongs survival, improve symptoms control and improves quality of life
(QoL). Treatment selection is based on multiple factors. The most important patients'
related factors for those who wish to proceed with palliative chemotherapy are PS and
com-morbidities. Histological tumour subtype, presence of EGFR, K-RAS mutations or
ALK/ROS1 fusions are the most important Tumor-related factors that significantly
changed the therapeutic options for molecularly selected patients with metastatic
NSCLC. Patient education about potential side effects and their management, especially
in regards to the new targeted agents, are an essential part of treatment planning.

The standard first-line therapy for patients with EGFR wild type tumours and without
ALK gene fusions that have ECOG PS of 0-2 is 4 to 6 cycles of platinum doublet
therapy. Gemcitabine/cisplatin is most commonly prescribed, however several
combinations have similar outcomes, including paclitaxel/carboplatin,
vinorelbine/cisplatin, and docetaxel/cisplatin (listed in Appendix III 3a).
Pemetrexed/cisplatin, although not currently funded through Cancer Care Ontario, is also
an important option in those with non-squamous histology. Carboplatin may be
substituted for cisplatin where patients are unable to tolerate cisplatin. Single agent
chemotherapy is reserved for very elderly or frail patients (Appendix III 3b).

Second-line chemotherapy with pemetrexed (non-squamous histology only) or docetaxel
is offered to good PS patients (Appendix III 3c). Those with non-squamous histology
who have received first-line pemetrexed/cisplatin are offered docetaxel second-line.
Treatment should be offered until progression, although currently funded for up to 6
cycles by Cancer Care Ontario.

After chemotherapy failure, in the second- or third-line setting, all patients are offered the
EGFR tyrosine kinase inhibitor erlotinib at a dose of 150 mg daily, with evidence of
improved survival and quality of life in unselected, pretreated patients with
advanced/metastatic NSCLC. The dose may be reduced to 100 mg daily if patients have
unbearable toxicity despite maximal supportive measures. Skin care, education and
appropriate supportive therapy for management of skin rash should be maximized prior to
dose reduction for skin toxicity.

Where the EGFR mutation status is known before initiating first-line therapy, gefitinib is
offered to EGFR mutation positive patients where funding is available, to be followed by
platinum-based doublet therapy upon progression, and subsequent pemetrexed,
(docetaxel if squamous histology). If EGFR status is unknown or pending, patients
should NOT be offered first-line gefitinib, for reasons of potential inferior outcome.

Maintenance therapy with pemetrexed improves survival in patients with non-squamous
NSCLC and stable or responding disease after 4 cycles of first-line platinum-based
doublet therapy, (not containing pemetrexed first-line). While not currently funded by
Cancer Care Ontario, pemetrexed maintenance is an important option for patients. Data

also exist to support early initiation of maintenance erlotinib. The following summarizes currently funded options.

If EGFR mutation status is negative or unknown:

First Line Chemotherapy:
Consideration of clinical trial, if available
Platinum combinations for 4 to 6 cycles
Single agent therapy if unable to tolerate platinum
Supportive Care (early referral to palliative care)

Second Line Therapy:
Consideration of clinical trial, if available
Single agent docetaxel if squamous histology, or previous pemetrexed
Pemetrexed if non squamous histology
Erlotinib if unable to tolerate further chemotherapy
Supportive Care

Third Line Treatment:
Erlotinib (ECOG 0-3)
Clinical Trial Entry
Supportive Care

If EGFR mutation status is positive:

Gefitinib 250 mg po daily may be used first-line if the patient has insurance coverage. Upon progression, patients are offered platinum doublet therapy, and then second-line chemotherapy. Patients are not offered fourth-line erlotinib.

Elderly patients (>70 yrs):
These patients may be considered for the above treatments depending on their PS. However toxicity may be enhanced in older adults and treatment toxicity may have a significant functional impact. Treatment for older adults must be considered individually at time of clinical assessment. Single agent therapy may be an option, and supportive care as well as consideration of geriatric assessment is important in this population.

Radiotherapy
Many patients with lung cancer have symptoms due to their thoracic or metastatic disease. If patients are asymptomatic radiotherapy (RT) may not be indicated, especially if chemotherapy is planned. Palliative RT is useful for the relief of symptoms, especially hemoptysis, chest pain, cough and dyspnea due to airway obstruction, superior vena cava (SVC) syndrome, spinal cord compression, and pain from bone metastases. Mass reduction by radiotherapy is often considered, e.g. for patients with palpable lymph nodes or brain metastases, even if those lesions are not causing symptoms or the symptoms were managed with other measures (e.g. steroids for brain edema). Reduction in tumor size, e.g. in brain metastases, may be useful in avoiding steroid toxicity, and preserving

neurological function. An important goal of palliative RT is to reduce the risk of anticipated problems such as airway of SVC obstruction, or development of a spinal cord compression, in asymptomatic patients where there is concern of the above complications based on the anatomic location of the tumor. It is worth remembering, however, that it is often not possible to predict where the symptoms will occur, or which aspects of the disease will become an issue, particularly in patients who have many sites of disease.

Palliative Radiotherapy doses include:
- 8-10 Gy single fraction to thorax (poor PS patients) or to uncomplicated bone metastases. Single fraction stereotactic RT (SRS) to solitary brain metastases delivers a higher dose (18-24 Gy, depending on size of metastasis)
- 20 Gy in 5 fractions (fr) to thorax, whole brain, spinal cord, complicated bone metastases, soft tissue masses, lymph nodes etc
- 30 Gy in 10 fr when more prolonged palliation is desired
- Rarely 36 Gy in 12 fr for thoracic disease (see discussion re palliation of stage III NSCLC)

Endobronchial Brachytherapy (High dose rate (HDR) brachytherapy)
This is used for symptoms control in patients who have had previous external beam radiotherapy delivered to the mediastinum (to tolerance dose of central structures) and disease has recurred within or around the bronchi. Usual dose is 1 or 2 applications of 8-10Gy with HDR, iridium, prescribed to 1cm from the source.

Surgery
Surgical input in Stage IV disease is usually reserved for palliative intervention for symptom management. This will include:
- Resection of brain metastases either solitary (for local control) or lesions causing mass effect that are not responding to steroid treatment
- Surgical stabilization and decompression of the spine for vertebral metastases causing spinal cord compression
- Endobronchial and endotracheal interventions, including debridement, stent or laser therapy for obstructing bronchial lesions causing collapse or haemoptysis
- Occasionally resection of other solitary metastases (e.g. adrenal) in well selected patients

Other Therapy:

Other therapies used in the management of NSCLC:

Interventional Radiology
1. SVC stent placement for management of symptomatic SVCO
2. IVC filters for management of symptomatic DVT, if anticoagulation is contraindicated
3. Esophageal stents and/or percutaneous feeding tubes if significant dysphagia

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6.2   Small Cell Lung Cancer (SCLC):

SCLC is an aggressive malignancy with a predilection for early spread. PET/CT scan is used for staging patients with apparent limited stage (LS)-SCLC. Management is determined by categorizing patients into limited (LS) and extensive (ES) stage. LS-SCLC is defined as "encompassable within a reasonable RT field". LS-SCLC is typically managed with 4 to 6 cycles of etoposide/cisplatin chemotherapy, early concurrent thoracic radiation then followed by prophylactic cranial irradiation (PCI). ES-SCLC is managed with 4 to 6 cycles of etoposide/cispatin chemotherapy followed by PCI in those patients without brain metastasis. There is currently no routine role for thoracic RT in ES-SCLC although this is the subject of on-going clinical trials. Patients should be considered for clinical trial opportunities whenever possible.

The management of relapsed SCLC depends on the location of the recurrence and time interval from previous treatment. Patients with late relapse following initial therapy have a better prognosis. Treatment options for recurrence may include chemotherapy (etoposide/platinum if the progression-free interval is ≥12 months), or second-line therapy with CAV (cyclophosphamide, doxorubicin, vincristine). Topotecan is an alternative option, although not funded by Cancer Care Ontario, as are clinical trials. These regimens are detailed in Appendix III 5a-b. Palliative RT may be used for symptomatic metastatic sites and in poor PS patients.

6.2.1 Surgery
There is no routine role for surgery in the management of LS-SCLC. However, surgery may play a role in managements in highly selected circumstances such as concern over mixed histology tumors, and definitive local therapy to a T1/T2 lesion in conjunction with chemotherapy, PCI and possibly mediastinal RT. Surgery may occasionally be used for salvage in patients with isolated local recurrence or a failure to respond to chemo radiotherapy. In patients who have an unexpected diagnosis of SCLC after surgical resection should be discussed in a multi-disciplinary setting. These patients will require chemotherapy, PCI and in many cases thoracic radiotherapy to the mediastinum.

6.2.2   Chemotherapy
Four to six cycles of cisplatin/etoposide (EP) is the standard chemotherapy for patients with limited or extensive stage small cell lung cancer. The regimen is cisplatin ($25mg/m^2$) and etoposide ($100mg/m^2$) days 1 to 3 every 21 days (detailed in Appendix III 5a.). In certain circumstances the cycle interval is increased to 28 days. In patients who are not able to tolerate cisplatin, carboplatin may be substituted. Cisplatin is preferred in the curative setting. Thoracic radiotherapy should ideally be given concurrently with cycle 1 or 2 of EP. The does and timing of chemotherapy should remain the same during RT as long as it is tolerated.

Elderly patients should also be considered for curative treatment based on their overall medical condition.

In the setting of relapsed or progressive disease patients may receive etoposide/cisplatin (in those with a longer progression-free interval) CAV, topotecan or clinical trial.

6.2.3   Radiation Therapy
In LS-SCLC thoracic radiotherapy should be delivered concurrently with chemotherapy ideally within the first 1 or 2 cycles. The dose of the thoracic radiotherapy should be either 40Gy in 15 fractions delivered once a day or 45Gy in 30 fractions twice-daily (1.5 bid, 6 hrs apart). Our standard in 45Gy in 30 fractions as this regimen was associated with best outcomes in RCTs. On-going clinical trials aim to address the optimal dose/fractionation schedule in LS-SCLC

Radiotherapy should be directed to all original sites of disease prior to treatment. Nodal irradiation may either be to sites of involved nodes as defined by CT, histology or PET or elective nodal irradiation may be used, especially if there is uncertainty regarding precise extent of original disease. Radiation therapy planning considerations for SCLC are the same as described in the section on NSCLC.

Prophylactic cranial irradiation (PCI) should be given to all patients with LS-SCLC 4-6 weeks after completion of chemotherapy in patients with no progression. The dose of PCI is 25Gy in 10 fractions.

In ES-SCLC thoracic irradiation is not routinely recommended. However, for patients who have responded well to chemotherapy consolidative thoracic RT may be used to minimizing risk of symptomatic progression in the area of original disease. Patients with a minimal burden of metastatic disease may be considered for combined chemoradiotherapy per LS-SCLC treatment. The patient population with ES-SCLC who may benefit from this more aggressive approach is controversial and is the subject of ongoing studies. Patients who do not respond well to chemotherapy and have thoracic disease requiring further treatment may receive palliative dose radiotherapy (30/10, 20/5, 10/1).

PCI (25Gy/10) for ES-SCLC patients with response to chemotherapy decreases the risk of brain metastases and prolongs survival.

Patients who have brain metastasis at presentation may be treated with whole brain radiotherapy before chemotherapy or chemotherapy with whole brain radiotherapy depending on the response to chemotherapy. Patient with a recurrence in the brain may receive whole brain radiotherapy (20/5 or 30/10). If patients experience brain recurrence after previous PCI (25/10) the dose of WBRT is generally 20/8. The role of SRS in patients with brain metastases in SCLC is less clearly defined than in patients with NSCLC. Patients with a thoracic recurrence may be treated or retreated with radiotherapy depending on previous treatments and the location of the recurrence.

Other Therapy:

Other therapies used in the management of SCLC:

High dose rate (HDR) brachytherapy
HDR brachytherapy is rarely used in SCLC however remains an option in the palliative setting.

Endobronchial Therapy
1. Laser or PDT
2. Surgical debridement

Interventional Radiology

SVC stent placement for SVCO is a commonly utilized management option.

6.3   ONCOLOGY NURSING PRACTICE

Refer to [general oncology nursing practices](#)

7.   SUPPORTIVE CARE

7.1   Patient Education

Patient education is an integral aspect of cancer management in the lung site group. In addition to one-on-ne education specific to the patient situation, there are a multitude of written educational materials that we provide to patients. There are general pamphlets on specific cancers and the main treatments including the Lung Cancer Patient Guide, published by Lung Cancer Canada, 2010. Many from the Canadian Cancer Society, some of which are available in multiple languages, which is useful given the fact that many of our patients do not speak English), as well as specific PMH created brochures that describe specific treatments (eg thoracic radiation, specific chemotherapy regiment etc), specific tests (eg PET scan) and specific symptoms (eg how to manage pain, or fatigue). The specific educational content is provided depending on the patient's diagnosis and management options. In addition, there is a library with resources available to the patient, including books, a Lung Cancer CD-ROM educational Resource and a librarian/patient educator who is available to search for specific information with the patient/family.

7.2   Psychosocial Care

Refer to [general oncology psychosocial care guidelines](#)

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7.3 Symptom Management

Lung cancer patients have a multitude of physical and emotional symptoms related to their disease, treatment and co-morbid condition. The common symptoms include pain, dyspnea, fatigue, nausea, vomiting, constipation, anxiety, depression etc. DART and ESAS (Distress Assessment and Response Tool and Edmonton Symptom Assessment System) are the screening tools used to identify the symptoms of most concern to the patient. They add to the clinical assessment of the patient made by the clinician at an individual attendance, but are also recorded serially at each attendance, to observe outcomes of interventions used. Patients answers are reviewed by the nurse and oncologists, symptom management guides are used in response to this screening and patients with significant burden of symptoms can be referred to appropriate services (eg palliative care, social work etc).

7.4 Clinical Nutrition

There is a dedicated dietician for the lung site group. Nutritional advice and support may be required if there has been a substantial weight loss prior to diagnosis, difficulties maintaining oral intake during combined modality treatment (due to esophageal toxicity) or patients with esophageal compression from their malignancy. Occasionally patients experience dysphasia following surgical interventions which may require nutritional intervention. The goals of nutritional support are to maintain patient's weight throughout treatment and improve any preexisting nutritional deficiencies.

7.5 Palliative Care

Refer to *general oncology palliative care guidelines*

7.6 Other

Patients with thoracic malignancies frequently develop deep venous thrombosis (DVT) and pulmonary emboli (PE). There is a Thrombosis clinic available at TGH for urgent referral and management of DVT & PE. Daily SQ injection of low molecular weight heparin is the therapy of choice in cancer patients with DVT/PE, for 6 months, or in the case of active incurable cancer, may be life-long. Inpatients who are not fully mobile are given prophylactic doses of subcutaneous heparin.

8. <u>FOLLOW-UP</u>

For patients treated with curative intent for which there are no curative salvage options, in the absence of symptoms, a history and physical examination and chest x-ray should be performed every 3 to 4 months during the first 2 years; every 6 months thereafter through year 5; and yearly thereafter. In cases where there is a suspicion of a recurrence, metastases or possibly a new primary, other tests may be indicated, such as CTs, MRI, bone scan, PET or bronchoscopy.

For patients treated with curative intent for which there are curative salvage options, in the absence of symptoms, a history and physical examination and CT Thorax/abdomen should be performed at regular intervals (every 6 – 12 months).

In patients treated with palliative intent follow-up should be individually tailored and coordinated with other medical professionals involved in the patient's care. Follow up at 4 to 12 weekly intervals are commonly used, depending on the patient's symptoms, treatment and pace of disease.

Smoking cessation and avoidance of occupational and environmental exposure to carcinogenic substances are recommended as effective interventions to reduce the risk of second primary NSCLC in curatively treated patients.

APPENDIX I – PATHOLOGICAL CLASSIFICATIONS OF LUNG CANCER

2004 WHO Classification for lung cancer:
I.   Epithelial tumors
- A.   Benign
  - 1.   Papillomas
  - 2.   Adenoma
- B.   Dysplasia/carcinoma in situ
- C.   Malignant
  - 1.   Squamous cell carcinoma
    - a.   Spindle cell variant
  - 2.   Small cell carcinoma
    - a.   Oat cell carcinoma
    - b.   Intermediate cell type
    - c.   Combined oat cell carcinoma
  - 3.   Adenocarcinoma
    - a.   Acinar
    - b.   Papillary
    - c.   Bronchioalveolar
    - d.   Solid carcinoma with mucin formation
  - 4.   Large cell carcinoma
    - a.   Giant cell carcinoma
    - b.   Clear cell carcinoma
  - 5.   Adenosquamous carcinoma
  - 6.   Carcinoid tumor
  - 7.   Bronchial gland carcinoma
  - 8.   Others

II.   Soft tissue tumors

III.   Mesothelial tumors
- A.   Benign
- B.   Malignant

IV.   Miscellaneous tumors
- A.   Benign
- B.   Malignant

V.   Secondary tumors

VI.   Unclassified tumors

VII. Tumorlike lesions

2011 IASLC/ATS/ERS Classification of Lung
Adenocarcinoma in Resection Specimens
   Preinvasive lesions:
     Atypical adenomatous hyperplasia
     Adenocarcinoma in situ (3 cm formerly bronchioloalveolar carcinoma or BAC)

Nonmucinous
Mucinous
Mixed mucinous/nonmucinous
Minimally invasive adenocarcinoma (3 cm lepidic predominant tumor with 5 mm invasion)
Nonmucinous
Mucinous
Mixed mucinous/nonmucinous
Invasive adenocarcinoma
Lepidic predominant (formerly nonmucinous BAC pattern, with 5 mm invasion)
Acinar predominant
Papillary predominant
Micropapillary predominant
Solid predominant with mucin production
Variants of invasive adenocarcinoma
Invasive mucinous adenocarcinoma (formerly mucinous BAC)
Colloid
Fetal (low and high grade)
Enteric

IASLC, International Association for the Study of Lung Cancer; ATS, American Thoracic Society; ERS, European Respiratory Society

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APPENDIX II

NSCLC and SCLC STAGING (Joint UICC & AJCC Staging Seventh Edition, 2010):

Primary Tumor (T)
TX Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0 No evidence of primary tumor
Tis Carcinoma in situ
T1 Tumor 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (for example, not in the main bronchus)1
T1a: Tumor 2 cm or less in greatest dimension
T1b: Tumor more than 2 cm but 3 cm or less in greatest dimension
T2: Tumor more than 3 cm but 7 cm or less or tumor with any of the following features (T2 tumors with these features are classified T2a if 5 cm or less): involves main bronchus, 2 cm or more distal to the carina; invades visceral pleura (PL1 or PL2); associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
T2a: Tumor more than 3 cm but 5 cm or less in greatest dimension
T2b: Tumor more than 5 cm but 7 cm or less in greatest dimension
T3: Tumor more than 7 cm or one that directly invades any of the following: parietal pleural (PL3), chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumor in the main bronchus less than 2 cm distal to the carina1 but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe
T4: Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe

Regional Lymph Nodes (N)
NX: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastases
N1: Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2: Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3: Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

Distant Metastasis (M)
M0 No distant metastasis
M1: Distant metastasis
M1a: Separate tumor nodule(s) in a contralateral lobe, tumor with pleural nodules or malignant pleural (or pericardial) effusion2
M1b: Distant metastasis (in extrathoracic organs)

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Stage Groupings:TNM Subsets

Occult carcinoma:	TX	NO	MO
Stage 0:	TIS	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
Stage IV:	AnyT	AnyN	M1a
	Any T	AnyN	M1b