NON-SMALL CELL LUNG CANCER
STAGE I
Effective Date: July, 2014

The recommendations contained in this guideline are a consensus of the Alberta Provincial Thoracic Tumour Team synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.
BACKGROUND

Lung cancer is the second most common cancer in both males and females in Canada. By the end of 2013, an estimated 25,500 new cases of lung cancer were diagnosed in Canada.\textsuperscript{1} In addition, lung cancer is the leading cause of cancer death for both sexes; an estimated 20,200 Canadian men and women died from their disease in 2013.\textsuperscript{1} While lung cancer death rates are decreasing among Canadian men, they continue to climb among Canadian women. Despite many research and clinical advances in lung cancer treatments, the age-standardized five-year survival rate for all types and stages of lung cancer combined is only 17 percent for Canada overall, and 14 percent for Alberta.\textsuperscript{2} The economic impact of lung cancer care is equally as staggering: the mean cost associated with the care of each patient diagnosed with lung cancer in Alberta has been reported to be $15,023 for non-small cell lung cancer and $18,243 for small cell lung cancer, not including end-of-life care.\textsuperscript{3} Smoking remains the largest single risk factor for lung cancer, and is responsible for 90 percent of lung cancers in men and 80 percent of lung cancers in women in Canada. Exposure to specific industrial and atmospheric pollutants, including second-hand tobacco smoke, also increases an individual’s risk of lung cancer.

GUIDELINE QUESTIONS

- What are the diagnostic workup recommendations for patients with stage I non-small cell lung cancer?
- What are the surgical recommendations for patients with stage I non-small cell lung cancer?
- Is adjuvant treatment recommended in patients with stage I non-small cell lung cancer?
- What are the recommendations for stereotactic body radiation therapy in patients with stage I non-small cell lung cancer?
- What are the recommendations for radiotherapy in patients with stage I non-small cell lung cancer?
- What are the follow-up and surveillance recommendations for patients with stage I non-small cell lung cancer?

DEVELOPMENT AND REVISION HISTORY

This guideline was reviewed and endorsed by the Alberta Provincial Thoracic Tumour Team. Members of the Alberta Provincial Thoracic Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Thoracic Tumour Team and a Knowledge Management Specialist from the Guideline Utilization Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook.

This guideline was originally developed in July, 2008. This guideline was revised in September, 2009, June, 2011 and July, 2014.

SEARCH STRATEGY

For this guideline update, two search strategies were used. The first was a general search using MEDLINE (1946 to January 30, 2014), EMBASE (1974 to January 30, 2014), PubMed (1975 to January 30, 2014), and the Cochrane Database of Systematic Reviews electronic databases; the references and bibliographies of articles identified through these searches were scanned for additional sources. The search terms were carcinoma, non small cell lung [MeSH] OR lung neoplasms [MeSH] AND stage I or
early stage [key term]. The search was limited to the following: clinical trial, all OR meta analysis OR randomized controlled trial OR systematic reviews. The working group excluded articles from the final review if they were not available through the library system.

The second strategy was more focused and used the MEDLINE (1946 to March 10, 2014), EMBASE (1974 to March 20, 2014), PubMed (1975 to March 20, 2014), and the Cochrane Database of Systematic Reviews electronic databases; the references and bibliographies of articles identified through these searches were scanned for additional sources. The search terms were SBRT OR stereotactic body radiation therapy OR SABR OR stereotactic ablative radiotherapy OR ablative radiotherapy [key terms] AND carcinoma, non small cell lung [MeSH] AND inoperable [key term]. The search was limited to the following: clinical trial, all OR meta analysis OR randomized controlled trial OR systematic reviews. The working group excluded articles from the final review if they were not available through the library system.

A search for new or updated practice guidelines published since June 2011 was also conducted.

The working group reviewed the currency and acceptability of all relevant literature and updated published guidelines for the treatment for stage I non-small cell lung cancer; we then circulated a draft of the updated guideline to the entire provincial tumour team for final feedback and approval.

TARGET POPULATION

The recommendations in this guideline apply to adult patients over the age of 18 years.

RECOMMENDATIONS

1. Surgical resection is the cornerstone of treatment and the best option for achieving cure in patients with clinically operable non-small cell lung cancer (NSCLC).

2. In circumstances where surgical resection may not be feasible, patients may be presented at a Multidisciplinary Tumour Board for further discussion between surgery, medical oncology, radiation oncology, nursing, palliative care and/or other disciplines as needed.

3. Whenever possible, patients should be considered for enrollment into clinical trials.

Diagnosis and Clinical Staging

4. PET-CT is recommended for all patients with suspected stage I NSCLC to rule out advanced disease.

5. Pulmonary function test is indicated for all surgical candidates.

6. Invasive staging for mediastinal lymph biopsy, via endobronchial ultrasound, mediastinoscopy, or VATS, is indicated for all patients with clinical stage T2Nx or TxN1/2 or greater disease to achieve pathological confirmation of true lymph node status. Please refer to the Non-Small Cell Lung Cancer Staging document for appropriate staging definitions.

7. Please also refer to the AHS Lung Cancer Requirements for a Referral to a Cancer Centre document for more information.

Surgery

8. Systematic mediastinal lymph node sampling or dissection should be performed for accurate pathologic staging of patients undergoing resection for stage I NSCLC.
9. Surgical resection is recommended for patients with clinical stage I NSCLC and no medical contraindications to operative intervention.
10. All patients with stage I disease should be evaluated by a thoracic surgeon to determine whether they are an appropriate candidate for surgery.
11. A lobectomy or anatomic pulmonary resection is recommended over a sublobar resection for patients with stage I NSCLC who are medically fit for surgery.
12. A sublobar resection is recommended over non-surgical interventions for patients with stage I NSCLC who cannot tolerate a lobectomy or anatomic pulmonary resection due to co-morbid disease or decreased pulmonary function.
13. For patients with an anatomically appropriate (central) tumour, a sleeve lobectomy is the preferred treatment; a pneumonectomy is an acceptable alternative.
14. Re-resection is recommended for patients with positive margins in resected stage I NSCLC; if re-resection is not possible, radiotherapy should be considered.
15. Patients who are inoperable or refuse surgery should be referred to a Radiation Oncologist for consideration of radiotherapy.

Adjuvant Chemotherapy

16. Postoperative chemotherapy is not recommended for patients with completely resected stage IA NSCLC.
17. Postoperative adjuvant chemotherapy may be considered in select individuals with resected stage IB NSCLC with tumours > 4 cm in diameter.
   - Cisplatin-based chemotherapy (i.e., cisplatin/vinorelbine) is the preferred treatment. A carboplatin-based chemotherapy regimen, such as carboplatin/paclitaxel, can be used as an alternative if there is a contraindication to cisplatin.
   - Chemotherapy should be administered within 12 weeks of surgical resection and ideally between 6 to 8 weeks.

Stereotactic Body Radiation Therapy

18. Stereotactic body radiation therapy (SBRT), when available, is recommended for patients with node negative tumours ≤ 5 cm who are medically inoperable or who decline surgery.
19. For peripheral tumours, the recommended dose is 48 Gy delivered in 4 fractions.
20. For central tumours, the recommended dose is 60 Gy delivered in 10 fractions or less, although dosing for central tumours is evolving.
21. Note: modification in dose fractionation may be required to ensure patient safety at the discretion of the Radiation Oncologist.

Radiotherapy

22. Radical radiation treatment may be considered if a patient is not a candidate for SBRT. SBRT is the preferred technique over conventionally fractionated radiotherapy, if available.

Follow-up and Surveillance

23. Follow-up for stage I NSCLC treated with curative intent therapy should involve one of the following protocols:
• A physical examination and chest x-ray every 3 months for 2 years post-treatment, then every 6 months for the third year post-treatment, then annually up to the fifth year post-treatment; the frequency is dependent on risk factors for recurrence and may be more or less frequent.

• A physical examination and high resolution CT scan every 6 months for the first 2 years and then a low-dose CT scan annually up to 5 years post-treatment; the frequency is dependent on risk factors for recurrence and may be more or less frequent.

24. Each follow-up visit should also include an assessment of the patient’s smoking status, as well as counseling and referral to smoking cessation programs.

**DISCUSSION**

**Diagnosis and Classification**

A PET-CT is indicated for all patients with suspected stage I NSCLC. Surgical candidates should also receive a pulmonary function test to ensure adequate lung function for resection. NSCLC accounts for 80 percent of all lung cancer cases, and is categorized using the seventh edition TNM staging system. In 2010, the Alberta Cancer Registry reported 864 patients with stage I NSCLC. The stage definitions and groups for NSCLC are summarized in a supporting document (Non-Small Cell Lung Cancer Staging).

**Surgery**

Systematic mediastinal lymph node sampling or dissection should be performed for accurate pathologic staging of patients undergoing resection for stage I NSCLC. In a pooled analysis of three studies comparing mediastinal lymph node dissection to systematic sampling, Manser and colleagues reported a significant reduction in the risk of death in patients with stages I to IIIA NSCLC undergoing dissection, with a pooled hazard ratio (HR) of 0.63 (95% CI 0.51-0.78; p<0.0001). Similarly, in a case series involving 100 consecutive patients, Lardinois et al. reported that mediastinal lymph node dissection was associated with longer disease-free survival and better local tumour control rates compared to mediastinal lymph node sampling after complete resection for N0-1 disease, with no increase in morbidity. In a prospective randomized trial completed by the American College of Surgery Oncology Group (ACOSOG Z0030 trial), the investigators also reported that morbidity is not increased with complete lymph node dissection, and recommended that the number of lymph nodes resected during mediastinal lymph node dissection be 12 or more, with nodes removed from stations 2R, 4R, 7, 8, 9 and 10R for right-sided cancers, and stations 4L, 5, 6, 7, 8, 9 and 10L for left-sided cancers. Published data from the ACOSOG study showed little difference in median survival between patients in the mediastinal lymph node sampling group compared to the dissection group (8.1 years vs. 8.5 years, p=0.25). Five-year disease-free survival rates were also similar (69% vs. 68%, p=0.92), and there were no differences in local, regional, or distant recurrences between the two groups. The investigators concluded that, for patients undergoing resection for N0 or nonhilar N1, T1, or T2 NSCLC, and for whom systematic and thorough presection sampling of the mediastinal and hilar lymph nodes is negative, mediastinal lymph node dissection does not improve survival in patients with early stage disease.

Surgical resection remains the treatment of choice for patients with early stage NSCLC, and offers the best potential for long-term survival and cure. All patients with early stage disease should be evaluated by a thoracic surgeon to determine whether they are an appropriate candidate for surgery. The likelihood of long-term survival without surgical resection is very low; a recent analysis from a cancer registry in the United States reported a 5 year overall survival rate of only 6 percent for patients with
untreated stage I disease. In contrast, the 5 year survival rate for patients with stage IA or IB disease who undergo surgical resection is commonly accepted to be between 60 and 80 percent.

**Lobectomy.** A lobectomy, the surgical removal of a single lobe, is the optimal procedure for the management of early stage disease. For patients who are medically fit for surgery, a lobectomy is preferred over a sublobar resection. This recommendation has been adopted from recommendations made by the American College of Chest Physicians (ACCP) and the National Comprehensive Cancer Network (NCCN). Conflicting results have been published in some retrospective reports and meta-analyses regarding the benefits of a lobectomy compared to a sublobar resection for patients with stage I disease that are medically fit for surgery. However, in the only prospective multi-centre randomized trial completed to date, the Lung Cancer Study Group reported the findings of 247 patients with peripheral T1N0 disease who underwent either a lobectomy or limited resection. The investigators observed a 75 percent increase in recurrence rates, 30 percent increase in overall death rate, and a 50 percent increase in the death rate caused by lung cancer in patients who underwent a limited resection compared to patients who underwent a lobectomy.

**Sublobar resection.** A sublobar resection is recommended over non-surgical interventions for patients with stage I NSCLC who cannot tolerate a lobectomy or anatomic pulmonary resection due to co-morbid disease or decreased pulmonary function. A sublobar resection can either be a segmentectomy, which is removal of one or more anatomical segments, or a non-anatomical wedge resection. While lobectomy is currently the standard of care for all medically fit stage I patients, recent evidence suggests that sublobar resection may be appropriate for some patients with a small (1 cm or less) peripheral nodule, or for patients with bronchioloalveolar carcinoma histology. An ongoing multi-centre randomized phase III trial (CALGB-140503) comparing lobectomy to sublobar resection in patients with small peripheral stage IA tumours may help clarify the role of sublobar resection as a primary treatment option for some patients.

Video-assisted thoracic surgery (VATS), by experienced surgeons, or open thoracotomy are both appropriate resection techniques for patients with stage I NSCLC who are appropriate surgical candidates. Results from several published series have reported both cure and complication rates with VATS lobectomy or segmentectomy similar to those with open thoracotomy. In a recent analysis of prospectively collected data, Flores and colleagues compared outcomes from 398 patients with stage IA disease who underwent a VATS lobectomy to 343 patients who underwent thoracotomy. The investigators reported similar 5-year survival rates for both procedures, but patients who underwent VATS lobectomy had fewer complications and shorter length of hospital stay than patients who underwent thoracotomy.

The surgical procedure used will depend on the extent of the disease, location of the tumour, and cardiopulmonary reserve of the patient. Members of the Alberta Provincial Thoracic Tumour Team agree with recommendations from both the NCCN and ACCP stating that for patients with an anatomically appropriate tumour, a sleeve lobectomy is the preferred treatment to pneumonectomy, in order to conserve lung function.

The members of the Alberta Provincial Thoracic Tumour Team recommend that patients with positive margins following resection of stage I disease should be considered for re-resection; for cases where additional surgery is not an option, tumour team members recommend radical radiotherapy.
Adjuvant Chemotherapy

A relatively small number of patients with stage IA disease have been included in randomized trials of adjuvant chemotherapy. In a meta-analysis of five large trials involving 4584 patients, the LACE collaborative group demonstrated a potential adverse effect of chemotherapy on patients with stage IA disease (HR for death=1.40; 95% CI 0.95-2.06). Based on these results, adjuvant chemotherapy is not currently recommended in patients with stage IA NSCLC.

There is ongoing debate on the benefit of adjuvant chemotherapy in patients with stage IB NSCLC. In an exploratory analysis from the CALGB 9633 trial, which focused exclusively on patients with stage IB disease (T2N0), the investigators reported a statistically significant survival benefit in stage IB patients with tumours ≥ 4 cm in diameter who were treated with carboplatin plus paclitaxel compared to observation (HR=0.69; 90% CI 0.48-0.99; p= 0.043). There was also a significant improvement in disease-free survival in favour of the chemotherapy group (HR=0.69; 90% CI=0.49-0.97, p<0.035). Similarly, in an updated analysis of the JBR.10 trial, Butts et al. reported a non-significant trend in favour of adjuvant vinorelbine plus cisplatin chemotherapy for patients with completely resected stage IB tumours ≥4cm in diameter (HR=0.66; 95% CI 0.39-1.14, p=0.13) Results from the LACE meta-analysis, however, did not demonstrate a survival advantage for stage IB patients treated with cisplatin-based regimens (HR=0.93; 95% CI 0.78-1.10). At the present time, members of the Alberta Provincial Thoracic Tumour Team agree that adjuvant chemotherapy should be considered on an individual basis for patients with stage IB disease, after a thorough evaluation of the risks and perceived benefits. In cases where adjuvant chemotherapy is indicated, tumour team members currently view the combination of cisplatin and vinorelbine as standard, based on results from the IALT, JBR.10, and ANITA clinical trials, as well as a subgroup evaluation from the LACE meta-analysis. The combination of carboplatin and paclitaxel, such as was used in the CALGB 9633 trial, is an acceptable alternative for individuals with a contraindication to cisplatin. Chemotherapy should ideally start 6 to 8 weeks post-surgery, but certainly before 12 weeks.

Stereotactic Body Radiation Therapy

Approximately 25 percent of patients with stage I NSCLC cannot or will not undergo surgery due to poor lung function, advanced age, comorbidities, or patient refusal. There is growing evidence that SBRT achieves superior survival as compared to treatment using conventionally fractionated RT for tumours ≤5 cm. The Alberta Provincial Thoracic Tumour Team agrees that SBRT is the preferred treatment modality for eligible patients, if available, over conventionally fractionated radiotherapy (see Radiotherapy section below). SBRT is a technique that delivers precisely targeted, high-dose radiation to a small or moderate-sized tumor while minimizing radiation to adjacent normal tissue. This targeting allows treatment of the tumour in either a single or limited number of dose fractions. The Alberta Provincial Thoracic Tumour Team recommends doses of either 60 Gy delivered in 10 fractions or less for central tumours, or 48 Gy delivered in 4 fractions for peripheral tumours although modification in dose fractionation may be required to ensure patient safety at the discretion of the Radiation Oncologist. SBRT has achieved high primary tumour control rates of over 90 percent.

A recent systematic review of SBRT for 563 central lung tumours, including 315 early-stage patients, found that local control rates were ≥ 85 percent when the prescribed biologically equivalent dose was ≥ 100 Gy. The study authors concluded that SBRT achieves high local control rates when appropriate fractionation schedules are used for central lung tumours.
There are a number of nonrandomized, prospective and population-based studies that have investigated SBRT for medically inoperable stage I NSCLC patients. Nearly all published series report local control rates of 85 to 95 percent as well as very low acute and late toxicity rates as compared to conventional RT (less than 4 percent grade 3 or higher toxicity reported). Table 1 below summarizes the results of prospective trials of SBRT for stage I NSCLC.

The optimal dose and schedule for SBRT in stage I NSCLC patients remains uncertain. Dose fractionation schemes differ between reported series and the optimal dose fractionation schedule may vary with tumor stage and location (see Appendix A). No randomized studies have compared different fractionation schemes to date. The suitability of SBRT as first-line treatment in operable patients has yet to be defined by randomized trials. Although data exists suggesting that high surgical risk patients (e.g., elderly, COPD patients, and patients with previous lung resections) may benefit most from a switch to SBRT for first-line treatment, given shorter hospital length of stay and increased quality of life.

Table 1. Results of Prospective Trials of SBRT for Stage I NSCLC

<table>
<thead>
<tr>
<th>Trial</th>
<th># patients</th>
<th>Stage</th>
<th>Median follow-up (months)</th>
<th>Dose (Gy), fractions</th>
<th>% toxicity ≥grade 3</th>
<th>Local control</th>
<th>Overall survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baumann et al. 2008&lt;sup&gt;35&lt;/sup&gt; Phase II</td>
<td>57</td>
<td>T1–2 N0 M0</td>
<td>35</td>
<td>45/3</td>
<td>30</td>
<td>3 yrs: 92%</td>
<td>3 yrs: 60%</td>
</tr>
<tr>
<td>Fakiris et al. 2009&lt;sup&gt;36&lt;/sup&gt; Phase II</td>
<td>70</td>
<td>T1–2 N0 M0</td>
<td>50.2</td>
<td>60–66/3</td>
<td>16</td>
<td>3 yrs: 88.1%</td>
<td>3 yrs: 42.7%</td>
</tr>
<tr>
<td>Grills et al. 2010&lt;sup&gt;37&lt;/sup&gt;</td>
<td>124</td>
<td>T1–2 N0 M0</td>
<td>30</td>
<td>48/4 or 60/5</td>
<td>11</td>
<td>NA</td>
<td>2.5 yrs: 72%</td>
</tr>
<tr>
<td>Koto et al. 2007&lt;sup&gt;38&lt;/sup&gt; Phase II</td>
<td>31</td>
<td>T1–2 N0 M0</td>
<td>32</td>
<td>45/3 or 60/8</td>
<td>3</td>
<td>2 yrs T1: 77.9%, T2: 40%</td>
<td>3 yrs: 71.7%</td>
</tr>
<tr>
<td>Le et al. 2006&lt;sup&gt;39&lt;/sup&gt; Phase I</td>
<td>32</td>
<td>T1–2 N0 M0</td>
<td>18</td>
<td>15–30/1</td>
<td>13</td>
<td>1 yr: 91% for dose ≥25 Gy</td>
<td>1 yr: 85%</td>
</tr>
<tr>
<td>Ricardi et al. 2010&lt;sup&gt;40&lt;/sup&gt; Phase II</td>
<td>62</td>
<td>T1–2 N0 M0</td>
<td>28</td>
<td>45/3</td>
<td>3</td>
<td>3 yrs: 87.8%</td>
<td>3 yrs: 57.1%</td>
</tr>
<tr>
<td>Shibamoto et al. 2012&lt;sup&gt;41&lt;/sup&gt;</td>
<td>180</td>
<td>T1–2 N0 M0</td>
<td>36</td>
<td>44 or 48 or 52/4</td>
<td>13</td>
<td>3 yrs: 86% (≤3 cm), 73% (&gt;3 cm)</td>
<td>3 yrs: 69%</td>
</tr>
<tr>
<td>Timmerman et al. 2006&lt;sup&gt;42&lt;/sup&gt; Phase II</td>
<td>70</td>
<td>T1–2 N0 M0</td>
<td>17.5</td>
<td>60–66/3</td>
<td>20</td>
<td>2 yrs: 95%</td>
<td>2 yrs: 54.7%</td>
</tr>
<tr>
<td>Timmerman et al. 2010&lt;sup&gt;43&lt;/sup&gt; Phase II</td>
<td>55</td>
<td>T1–2 N0 M0</td>
<td>34.4</td>
<td>60/3</td>
<td>16</td>
<td>3 yrs: 97.6%</td>
<td>3 yrs: 55.8%</td>
</tr>
<tr>
<td>Zimmerman et al. 2006&lt;sup&gt;44&lt;/sup&gt; Phase I/II</td>
<td>68</td>
<td>T1–2 N0 M0</td>
<td>17</td>
<td>24–40/3–5</td>
<td>3</td>
<td>3 yrs: 88%</td>
<td>3 yrs: 53%</td>
</tr>
</tbody>
</table>
Radiotherapy

Radical radiotherapy remains an important treatment option for patients with early stage NSCLC who are not candidates for SBRT. In one randomized trial of 169 patients with stages I and II disease, continuous hyperfractionated accelerated radiotherapy (CHART; 1.5 Gy three times daily/12 days) resulted in superior survival rates when compared to conventional fractionated radiotherapy (60Gy/30 fractions over 6 weeks). However, CHART is often not a feasible option due to lack of equipment and manpower, as well as low patient compliance. In a systematic review of one randomized and 26 non-randomized studies, Rowell and colleagues concluded that when CHART is not available, patients with early stage NSCLC who are medically inoperable but suitable for radical radiotherapy should be offered fractionated radiotherapy.

Patients with early-stage NSCLC who are medically inoperable and not suitable for radical radiotherapy should be offered palliative radiotherapy for symptom management, when appropriate. Detailed recommendations can be found in the Palliative Radiotherapy Clinical Practice Guideline.

Follow-up and Surveillance

The incidence of local recurrence following surgical resection of early stage NSCLC was documented in an 11-year study of 975 consecutive patients treated at a single institution. In this study, a local failure was defined as a recurrence at the surgical margin, in the ipsilateral hilum, or in the mediastinum. The 5-year incidence of any local recurrence after surgery was 23 percent, with a median time to recurrence of 14 months. In addition, the 5-year risk of any treatment failure, including local or distant relapses and second primary lung cancers, was 42 percent. First sites of recurrence were local only in 25 percent of cases, local and distant in 29 percent of cases, and distant only in 46 percent of cases.

Due to high rates of post-treatment recurrence, long-term follow-up and surveillance is recommended for patients with early stage NSCLC. To date there are no randomized trials assessing different surveillance strategies in patients with stage I NSCLC. One prospective study examined the feasibility and impact on patient survival of an intensive surveillance program of 192 NSCLC patients. The follow-up consisted of physical examination and chest roentgenogram every 3 months and fiberoptic bronchoscopy and thoracic CT scan with sections of the liver and adrenal glands every 6 months. Seventy-one percent of patients developed a recurrence; 26 percent were asymptomatic of which all but one were detected by a scheduled follow-up procedure. From the date of recurrence, 3-year survival was 13 percent in all patients and 31 percent in asymptomatic patients whose recurrence was detected by a scheduled follow-up procedure. The study authors concluded that intensive follow-up and surveillance may improve survival through early detection of potentially curable recurrences. The members of the Alberta Provincial Thoracic Tumour Team recommend that patients undergo a physical examination and chest x-ray every 3 months for the first year post-treatment, then every 6 months for the second year post-treatment, then annually up to the fifth year post-treatment.

Debate exists regarding the sensitivity and specificity of CT scans in identifying post-treatment changes, as well as the appropriate protocols for the use of CT scans to distinguish between benign and malignant nodules without excess morbidity and cost. As a result, various guideline publications and consensus statements differ in their recommendations regarding follow-up schedules and types of imaging required for patients treated with curative intent. The NCCN recommends a chest CT ± contrast every 6 to 12 months for 2 years, then non-contrast-enhanced chest CT annually. Similarly, the American Association for Thoracic Surgery recommends high-resolution chest CT scans every 6 months for 4 years after surgical
resection, followed by annual low-dose CT scans for the remainder of the patient’s life as long as they have functional status and pulmonary reserve needed to treat a new lung cancer.\textsuperscript{55} Given the state of the current evidence, the members of the Alberta Provincial Thoracic Tumour Team suggest that an alternative surveillance regimen be a high-resolution CT scan every 6 months for the first 2 years and then a low-dose CT scan annually up to 5 years post-treatment; the frequency is dependent on risk factors for recurrence and may be more or less frequent.

Smoking cessation also increases the efficacy of treatment, decreases the risk of complications, and reduces the risk of second primary malignancies; therefore each follow-up visit should also include an assessment of the patient’s smoking status, as well as counseling and referral to smoking cessation programs.\textsuperscript{13,52-54} Health care professionals, patients, and caregivers can refer to AlbertaQuits for smoking cessation information and resources.
TREATMENT ALGORITHM

Diagnosis & Clinical Staging
- PET-CT
- Pulmonary function test
- Mediastinal lymph biopsy, via endobronchial ultrasound, mediastinoscopy, or VATS, is indicated for all patients with clinical stage T2N0 or T2N1/2 or greater disease

Operable
- Systematic mediastinal lymph node sampling or dissection
- Patient status?
  - Medically fit
    - Lobectomy or Anatomic Pulmonary Resection
      - Sleeve lobectomy (preferred)
      - Pneumonectomy
    - Sublobar Resection
      - Segmentectomy
      - Wedge resection
  - Co-morbid disease, decreased pulmonary function
    - Assess for appropriateness of adjuvant chemotherapy for patients with stage IB disease

Assess for suitability of resection by thoracic surgeon

Inoperable/decline surgery
- Assess for suitability of SBRT
  - Suitable
  - Radical RT
    - Indicated for patients who are not candidates for SBRT
  - Not suitable
    - Refer to Radiation Oncologist

Follow-up & Surveillance
- Physical exam & chest x-ray or CT scan (see text for timing recommendations)
- Smoking cessation counseling

Positive margins after surgery?
  - Yes
    - Assess for suitability of re-resection
      - Suitable
        - Re-resection
      - Not suitable
        - Refer to Radiation Oncologist
  - No

In circumstances where surgical resection may not be feasible, patients may be presented at a Multidisciplinary Tumour Board for further discussion between surgery, medical oncology, radiation oncology, nursing, palliative care and/or other disciplines as needed.

Whenever possible, patients should be considered for eligibility in ongoing clinical trials.
GLOSSARY OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>AACP</td>
<td>American College of Chest Physicians</td>
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<tr>
<td>ACOSOG</td>
<td>American College of Surgery Oncology Group</td>
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<tr>
<td>ANITA</td>
<td>Adjuvant Navelbine International Trialists Association study</td>
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<tr>
<td>CALGB</td>
<td>Cancer and Leukemia Group B</td>
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<tr>
<td>CHART</td>
<td>continuous hyperfractionated accelerated radiation therapy</td>
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<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography scan</td>
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<tr>
<td>Gy</td>
<td>grey</td>
</tr>
<tr>
<td>HR</td>
<td>hazard ratio</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography scan</td>
</tr>
<tr>
<td>IALT</td>
<td>International Adjuvant Lung Trial</td>
</tr>
<tr>
<td>JBR.10</td>
<td>National Cancer Institute of Canada Clinical Trials Group trial # JBR.10</td>
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<tr>
<td>LACE</td>
<td>Lung Adjuvant Cisplatin Evaluation trail</td>
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<tr>
<td>NCCN</td>
<td>National Comprehensive Cancer Network</td>
</tr>
<tr>
<td>NSCLC</td>
<td>non-small cell lung cancer</td>
</tr>
<tr>
<td>PET</td>
<td>positron emission tomography scan</td>
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<tr>
<td>PFT</td>
<td>pulmonary function testing</td>
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<tr>
<td>PS</td>
<td>performance status</td>
</tr>
<tr>
<td>RT</td>
<td>radiotherapy</td>
</tr>
<tr>
<td>SBRT</td>
<td>stereotactic body radiotherapy</td>
</tr>
<tr>
<td>TNM</td>
<td>tumour-node-metastasis</td>
</tr>
<tr>
<td>VATS</td>
<td>video-assisted thoracic surgery</td>
</tr>
<tr>
<td>VQ</td>
<td>ventilation/perfusion scan</td>
</tr>
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</table>

DISSEMINATION

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

MAINTENANCE

A formal review of the guideline will be conducted at the Annual Provincial Meeting in 2016. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

CONFLICT OF INTEREST

Participation of members of the Alberta Provincial Thoracic Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Thoracic Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.
REFERENCES


# APPENDIX A: Common Doses for SBRT

<table>
<thead>
<tr>
<th>Tumour Size &amp; Location</th>
<th>Total Dose (Gy)</th>
<th># Fractions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral, &lt;2 cm</td>
<td>25 to 34</td>
<td>1</td>
</tr>
<tr>
<td>&gt;1 cm from chest wall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1 cm from chest wall</td>
<td>45 to 60</td>
<td>3</td>
</tr>
<tr>
<td>Central or peripheral, &lt;4 to 5 cm</td>
<td>48 to 50</td>
<td>4</td>
</tr>
<tr>
<td>&lt;1 cm from chest wall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central or peripheral</td>
<td>50 to 55</td>
<td>5</td>
</tr>
<tr>
<td>&lt;1 cm from chest wall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central</td>
<td>60 to 70</td>
<td>8 to 10</td>
</tr>
</tbody>
</table>

Table modified from the NCCN Guidelines: Non-Small Cell Lung Cancer Version 3.2014