Triple modality therapy with complete resection of locally advanced T4 Pancoast tumors with involvement of the spine offers an advantage to other therapeutic modalities or therapies with incomplete resections.

Management of Locally Advanced Pancoast (Superior Sulcus) Tumors With Spine Involvement
Matthias Setzer, MD, Lary A. Robinson, MD, and Frank D. Vrionis, MD, PhD

Background: The preferred treatment for locally aggressive lung cancers is triple modality therapy with concurrent and induction chemotherapy with radiation therapy followed by surgery. Patients with locally advanced T4 Pancoast tumors with spine involvement, without mediastinal N2 lymph node involvement and without distant metastases, are appropriate candidates for complete resection with subsequent spine reconstruction. This review addresses the questions of whether triple modality therapy with complete en bloc resection of locally advanced Pancoast tumors offers an advantage in terms of overall survival and complication rates compared with other therapeutic modalities or therapies with incomplete resection.

Methods: A comprehensive literature search was conducted using common medical databases. Inclusion and exclusion criteria for the articles were prospectively defined. The articles were independently reviewed and a consensus decision was made about each article. Selected papers were graded by level of evidence.

Results: A total of 1,001 abstracts and 93 articles fulfilled the criteria; from these studies, 14 were included in this systematic review. No level 1 study was found in this search. Four level 2 studies and 10 level 3 retrospective case series were found. The overall 5-year survival rate reported in these studies ranged from 37% to 59% and the mortality rate ranged from 0% to 6.9%.

Conclusions: Evidence suggests that triple modality therapy with complete resection of locally advanced Pancoast tumors with involvement of the spine offers an advantage over other therapeutic modalities or therapies with incomplete resections.
Introduction
The estimated world incidence of lung cancer is 1.35 million new cases every year the estimated annual mortality rate is 1.18 million deaths—of these, the highest rates of death are found in North America and Europe.1,2 Pancoast tumors account for 3% to 5% of all non–small-cell lung carcinomas (NSCLCs), or approximately 7,000 cases per year in the United States.4

Pancoast tumors are primary lung carcinomas arising from the apex of the lung and are generally located in the superior pulmonary sulcus. In most cases, Pancoast tumors are NSCLCs, most commonly squamous cell (52%), followed by adenocarcinomas (23%) and large cell carcinomas (20%); only about 5% of Pancoast tumors are of small cell origin.5,7

Pancoast tumors may extend in 3 directions8:
• Anteriorly by invading major blood vessels (eg, subclavian artery)
• Superiorly by primarily invading the brachial plexus
• Medially by invading the stellate ganglion, vertebral bodies, or mediastinal structures

Pancoast tumors cause characteristic symptoms, such as arm, shoulder, or scapular pain, radicular pain and muscle weakness in the distributions of the C8, T1, and T2 nerve roots, and Horner's syndrome (ptosis, miosis, and anhidrosis), when the sympathetic chain is involved.4,9 This symptom complex is also called Pancoast syndrome and includes ipsilateral anhidrosis, which is in contrast to lesions above the carotid bifurcation lacking this feature. In questionable cases, instilling cocaine drops in the affected eye will not cause pupillary dilation if Horner's syndrome is present.

Nerve root involvement must be differentiated from ulnar neuropathy, cervical radiculopathy (at C7–T1), intramedullary processes (syringomyelia, spinal cord tumors), and motor neuron disease, such as amyotrophic lateral sclerosis, which may occasionally start with atrophy of the intrinsic muscles of the hand. Pancoast tumors typically compress or invade the medial cord of the brachial plexus (C8, T1), giving rise to hand weakness and hypesthesia in the medial arm and forearm. Because it may be difficult to preoperatively differentiate between compression and invasion, patients with C8 symptoms should not be excluded from surgery based on clinical grounds alone. The absence of fasciculations and sensory findings excludes amyotrophic lateral sclerosis, while the absence of numbness in the medial arm and forearm excludes ulnar neuropathy. It is not uncommon to see patients with Pancoast tumors who previously underwent anterior cervical disectomies and fusions for tumor symptoms, and who thus then lacked improvement.

Pancoast tumors invading the mediastinal pleura, chest wall, and spine were previously considered generally unresectable and had an overall poor prognosis; radiotherapy alone or in combination with chemotherapy was the only available therapeutic option.10 However, newer therapies have improved the overall prognosis, leading to some cure and long-term survival rates. Researchers for a phase 2, non-randomized, intergroup Pancoast tumor trial added chemotherapy to induction radiation therapy followed by resection.11,12 Based on better results with this course of therapy, this regimen was adopted as the current standard of care. However, due to significant limitations, including wound-healing issues, poor tolerance to concurrent chemoradiotherapy in debilitated patients with Pancoast tumors, and the low tolerance of postoperative chemotherapy, alternative treatment strategies were developed.4 Several major cancer centers favor a sequential triple modality–therapy with induction chemotherapy or with a platinum doublet for 3 cycles (generally tumor pain lessens or resolves within 7–10 days after the start of chemotherapy), surgical resection 3 to 5 weeks after completing chemotherapy, followed by full-dose radiotherapy (6600 cGy) to the tumor bed, which is tumoricidal for close margins and any residual microscopic disease.4,15

The recent progress of spinal instrumentation—in addition to the development of reliable hardware and a wider acceptance of total “en bloc” spondylectomy—makes radical surgical modalities feasible.4,14 Because an incomplete resection is considered a poor prognostic factor, recent studies have focused on exploring the use of extended operations to achieve complete resection of Pancoast tumors invading the spine.15,16 The aim of the present article is to systematically review the literature and focus on the current multimodality treatment of locally advanced Pancoast tumors with spinal involvement.

Systematic Literature Review
A systematic review was designed to answer these questions:
1. Does triple modality therapy with complete resection of locally advanced T4 Pancoast tumors offer an advantage in terms of overall survival compared with other therapeutic strategies?
2. Does triple modality therapy with complete resection of locally advanced T4 Pancoast tumors offer an advantage in terms of complication rate compared with other therapies?

A comprehensive literature search was conducted using MEDLINE, EMBASE, Paper First, Web of Science, Google Scholar, and the Cochrane Database of Systematic Reviews. The MEDLINE search terms included the terms “Pancoast tumors” and “superior pulmonary sulcus tumors.”
Inclusion criteria were as follows: articles published between 1980 and 2013, articles written in either English, French, German, Italian, Japanese, Portuguese, Russian, or Spanish; had an adult age group (≥ 18 years); case series; and review articles. Exclusion criteria included articles focusing on primary spine or intradural tumors, tumors in a pediatric population, case reports with mixed pathology (e.g., tumor plus trauma plus degeneration), or studies with data insufficient to extract pertinent information about the tumor population. Articles reporting on treatments other than trimodality therapy (induction chemotherapy followed by radiation and surgery) were also excluded. Two independent reviewers screened the abstracts of all articles matching the search terms and inclusion/exclusion criteria. The screeners reviewed the full-text versions of suitable articles, which were then studied for information relevant to the research questions; their bibliographies were then searched for any additional references missed in the original literature search. Any disagreement on the selection of articles was resolved by discussion between the 2 reviewers. Selected papers were graded by level of evidence according to Sackett criteria.17 The results of the literature search are tabulated in Table 110,18-23 and Table 2.12,24-29

A total of 1,001 abstracts and 93 articles fulfilled the inclusion criteria. From these papers, 14 studies were included in the systematic review. No level 1 study was found in this search. Four level 2 studies were found, comprising 256 patients (76 patients with spinal involvement), as well as 10 level 3 studies (retrospective case series), including a total of 726 patients (299 patients with spinal involvement). Three level 3 studies exclusively used trimodality protocols (120 patients, 22 with spinal involvement). The remaining level 3 studies used various types of neoadjuvant therapy in addition to trimodality therapy.

### Table 1. — Selected Studies With Neoadjuvant Therapy Plus Trimodality Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Total No. of Patients</th>
<th>No. of Patients With Spinal Involvement</th>
<th>No. of Resections</th>
<th>5-Year Survival (%)</th>
<th>Median Survival (mos)</th>
<th>Postoperative Mortality Rate (%)</th>
<th>Complications (%)</th>
<th>Questions</th>
<th>1a</th>
<th>2a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alifano et al18</td>
<td>67</td>
<td>6</td>
<td>55</td>
<td>12</td>
<td>Complete: 45</td>
<td>NA</td>
<td>9</td>
<td>NA</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Attar et al10</td>
<td>105</td>
<td>64</td>
<td>55</td>
<td>12</td>
<td>26</td>
<td>20.8</td>
<td>NA</td>
<td>NA</td>
<td>Not applicable</td>
<td>N</td>
</tr>
<tr>
<td>Koizumi et al19</td>
<td>16</td>
<td>7</td>
<td>11</td>
<td>5</td>
<td>Complete: 59</td>
<td>NA</td>
<td>0</td>
<td>NA</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Komaki et al20</td>
<td>143</td>
<td>76</td>
<td>33</td>
<td>29</td>
<td>Complete: 55</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Yc</td>
<td>N</td>
</tr>
<tr>
<td>Martinod et al21</td>
<td>139</td>
<td>52</td>
<td>113</td>
<td>26</td>
<td>35</td>
<td>NA</td>
<td>7.2</td>
<td>NA</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Rusch et al22</td>
<td>101</td>
<td>62</td>
<td>T3: 46</td>
<td>T4: 5</td>
<td>—</td>
<td>13</td>
<td>12</td>
<td>4</td>
<td>NA</td>
<td>Y</td>
</tr>
<tr>
<td>Wright et al23</td>
<td>35</td>
<td>10</td>
<td>RT: 16</td>
<td>RT + CT: 14</td>
<td>—</td>
<td>RT: 49</td>
<td>48</td>
<td>NA</td>
<td>NA</td>
<td>N</td>
</tr>
</tbody>
</table>

All studies carried level of evidence III according to Sackett criteria.17

1a Question 1: Does triple modality therapy with complete resection of locally advanced T4 Pancoast tumors offer an advantage in terms of overall survival compared with other therapeutic strategies?

2a Question 2: Does triple modality therapy with complete resection of locally advanced T4 Pancoast tumors offer an advantage in terms of complication rate compared with other therapies?

c For patients with negative nodes.

CT = chemotherapy, N = no, NA = not available, RT = radiation therapy, Y = yes.
reported overall 5-year survival rates in these studies ranged from 37% to 59% and the mortality rates ranged from 0% to 6.9% (Table 1\(^{10,18-23}\) and Table 2\(^{12,24-29}\)).

The introduction of combined concurrent chemotherapy with radiotherapy as induction therapy has significantly increased survival rates in patients with Pancoast tumors compared with radiotherapy alone.\(^{10,18-23}\) Although level 1 studies do not exist, newer studies that exclusively use neoadjuvant chemotherapy plus radiation therapy as part of trimodality protocols have confirmed the safety and feasibility of these treatment strategies and have shown improved survival rates in patients with complete resections. Furthermore, the treatment was well tolerated with acceptable rates of mortality and morbidity.\(^{12,24-28}\)

Other studies suggest that trimodality therapies using induction chemotherapy and surgery followed by full-dose postoperative radiation therapy avoid the drawbacks of preoperative radiation therapy and are well tolerated, safe, and have good survival rates.\(^{13,20}\) However, which trimodality therapy is best for locally advanced Pancoast tumors is unclear. This is a question best addressed in large randomized trials, but, because of the rarity of the disease, it is unlikely such trials will be feasible.

Tumor-Node-Metastasis Classification System

Pancoast tumors are classified according to the tumor-node-metastasis (TNM) system of the American Joint Committee on Cancer and the International Union Against Cancer.\(^{30-32}\) Due to the peripheral location and involvement of the chest wall in Pancoast tumors, most are classified as T3 tumors or higher, typically invading resectable areas of the chest wall or superficially extending into the mediastinum. Further invasion of the brachial plexus, mediastinal structures, or the vertebral bodies classifies them as T4 tumors, which are less readily resectable (Figure). Table 3 provides an overview of the seventh revision of the TNM descriptors for staging NSCLC developed by the International Association for the Study of Lung Cancer and adopted by the International Union Against Cancer.\(^{30-32}\) Based on this staging classification, Pancoast tumors are either stage IIb or IIIa (T3N0-1; T4N0-1) in the absence of mediastinal N2 node involvement or distant metastasis.

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**Table 2.** — Selected Studies With Trimodality Therapy Alone

<table>
<thead>
<tr>
<th>Study</th>
<th>Level of Evidence</th>
<th>Total No. of Patients</th>
<th>No. of Patients With Spinal Involvement</th>
<th>No. of Complete Resections</th>
<th>5-Year Survival (%)</th>
<th>Median Survival (mos)</th>
<th>Complications (%)</th>
<th>Mortality Rate (%)</th>
<th>Questions 1 &amp; 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fischer et al(^{24})</td>
<td>III</td>
<td>44</td>
<td>14</td>
<td>39</td>
<td>34</td>
<td>5</td>
<td>54.5</td>
<td>2.6</td>
<td>N, Y</td>
</tr>
<tr>
<td>Goldberg et al(^{25})</td>
<td>III</td>
<td>39</td>
<td>3</td>
<td>39</td>
<td>34</td>
<td>5</td>
<td>47.9</td>
<td>6.9</td>
<td>N, Y</td>
</tr>
<tr>
<td>Kappers et al(^{26})</td>
<td>II</td>
<td>39</td>
<td>18</td>
<td>76</td>
<td>20</td>
<td>5</td>
<td>37</td>
<td>3.5</td>
<td>Y, N</td>
</tr>
<tr>
<td>Kunitoh et al(^{27})</td>
<td>II</td>
<td>76</td>
<td>20</td>
<td>54</td>
<td>37</td>
<td>5</td>
<td>10.5</td>
<td>13.6</td>
<td>N, Y</td>
</tr>
<tr>
<td>Kwong et al(^{28})</td>
<td>III</td>
<td>37</td>
<td>6</td>
<td>31</td>
<td>29</td>
<td>5</td>
<td>31.6</td>
<td>2.7</td>
<td>Y, N</td>
</tr>
<tr>
<td>Marra et al(^{29})</td>
<td>III</td>
<td>31</td>
<td>6</td>
<td>110</td>
<td>6</td>
<td>5</td>
<td>46</td>
<td>6.9</td>
<td>N, Y</td>
</tr>
<tr>
<td>Rusch et al(^{12})</td>
<td>II</td>
<td>110</td>
<td>32</td>
<td>110</td>
<td>6</td>
<td>5</td>
<td>46</td>
<td>6.9</td>
<td>Y, N</td>
</tr>
</tbody>
</table>

- Question 1: Does triple modality therapy with complete resection of locally advanced T4 Pancoast tumors offer an advantage in terms of overall survival compared with other therapeutic strategies?
- Question 2: Does triple modality therapy with complete resection of locally advanced T4 Pancoast tumors offer an advantage in terms of complication rate compared with other therapies?

Levels of evidence according to Sacket et al\(^{17}\): level II evidence, systematic review of cohort studies, cohort studies, and low-quality randomized control trials; level III evidence, retrospective case series.
Surgical Classification

Although the TNM staging system helps in general decision-making, it cannot be used to determine the extent of vertebral body resection, the operative approach, and whether or not instrumentation is needed. Therefore, spine surgeons have developed a classification of vertebral involvement to facilitate surgical planning.4,14,33

Type A Tumors

Type A tumors involve the transverse process and extend to but not beyond the neural foramina. The tumor may be attached to the vertebral body, but the tumor has not infiltrated it.

Type B Tumors

Type B tumors extend beyond the neural foramina into the epidural space and may cause cord compression and involve at least 1 root. The vertebral body is infiltrated or destroyed, but no more than one-third of the vertebral body is affected. These tumors require partial vertebral body resection and posterior instrumentation.

Type C Tumors

Type C tumors have vertebral body involvement of more than one-third in at least 1 level. In addition to vertebral body involvement, nerve root, cord compression, or both are also found.4 Anterior vertebral body reconstruction, together with posterior instrumentation, is typically performed.

Therapeutic Management

The management of Pancoast tumors has changed over the last decades. Before the introduction of radiation treatment in 1954 and the first successful removal of a Pancoast tumor with postoperative adjuvant radiation, the lung cancer was uniformly fatal.10,34 In 1961, Shaw et al35 published the first clinical series that used preoperative neoadjuvant radiation, demonstrating improved tumor resectability and long-term survival rates,5,36 making neoadjuvant radiation and surgical resection the standard method for the management of Pancoast tumors. Five-year survival rates range from 27% to 46% for tumors up to stage IIB.22,23

Table 3. — TNM Staging of Non–Small-Cell Lung Cancer

<table>
<thead>
<tr>
<th>6th ed. Descriptor</th>
<th>7th ed. Revised Descriptor</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 (≤ 2 cm)</td>
<td>T1a</td>
<td>IA</td>
<td>IIA</td>
<td>IIIA</td>
<td>IIIB</td>
</tr>
<tr>
<td>T1 (&gt; 2–3 cm)</td>
<td>T1b</td>
<td>IA</td>
<td>IIA</td>
<td>IIIA</td>
<td>IIIB</td>
</tr>
<tr>
<td>T2 (≤ 5 cm)</td>
<td>T2a</td>
<td>IB</td>
<td>IIA</td>
<td>IIIA</td>
<td>IIIB</td>
</tr>
<tr>
<td>T2 (&gt; 5–7 cm)</td>
<td>T2b</td>
<td>II A</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIB</td>
</tr>
<tr>
<td>T2 (&gt; 7 cm)</td>
<td>T3</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIA</td>
<td>IIIB</td>
</tr>
<tr>
<td>T3 invasion</td>
<td>T3</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIA</td>
<td>IIIB</td>
</tr>
<tr>
<td>T4 (same lobe nodules)</td>
<td>T3</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIA</td>
<td>IIIB</td>
</tr>
<tr>
<td>T4 (extension)</td>
<td>T4</td>
<td>IIIA</td>
<td>IIIA</td>
<td>IIIB</td>
<td>IIIB</td>
</tr>
<tr>
<td>M1 (ipsilateral lung)</td>
<td>T4</td>
<td>IIIA</td>
<td>IIIA</td>
<td>IIIB</td>
<td>IIIB</td>
</tr>
<tr>
<td>T4 (pleural effusion)</td>
<td>M1a</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
</tr>
<tr>
<td>M1 (contralateral lung)</td>
<td>M1a</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
</tr>
<tr>
<td>M1 (distant)</td>
<td>M1b</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
</tr>
</tbody>
</table>

Cells in bold and red indicate a change from the sixth to the seventh edition of the TNM Classification of Malignant Tumors for a particular TNM category.

TNM = tumor-node-malignancy.

Whether the tumor is attached to the vertebral column (demonstrated by radiographic findings)

- Presence or absence of mediastinal nodal involvement
- Presence or absence of distant metastasis

Generally, patients with locally advanced NSCLC of the superior sulcus, without mediastinal N2 to N3 lymph node involvement and without distant metastases, are considered appropriate candidates for surgical therapy. If the decision to proceed with surgery is made, then the appropriate approach must be selected. Such a selection is usually made on the basis of magnetic resonance imaging (MRI) and computed tomography (CT) studies of the chest. MRI is important to reveal or rule out tumor growth through the neural foramina into the spinal canal with resulting spinal cord compression. Using MRI and CT scans, it should be possible to assign the tumor to 1 of 3 spine tumor types to make the appropriate decision concerning the need for vertebral body resection and, if necessary, how much of the vertebral body must be resected (partial vs complete vertebrectomy).

If spinal stabilization is necessary, then it must be decided which approach is most appropriate and whether the procedure should be staged. The initial evaluation should include a thorough physical examination, including a detailed neurological examination, contrast-enhanced CT scans of the chest with 3-dimensional reconstructions, MRI with contrast of the thorax (including the brachial plexus and thoracic inlet), fusion positron emission tomography (PET)/CT scan, MRI of the brain, pulmonary function tests, standard laboratory tests, and possibly a stress test, depending on cardiac risk factors.

The use of standard CT scanning with intravenous contrast material to evaluate the mediastinum for lymph node metastases is limited by substantial false-positive and false-negative results, with pooled estimates of sensitivity and specificity rates of 51% and 85%, respectively. Newer-generation fusion PET/CT scans have improved the accuracy of mediastinum staging, with sensitivity and specificity rates of 74% and 85%, respectively. With equivocal lymph node enlargement (1.5-cm diameter nodes on the short axis), surgeons generally recommend an invasive assessment of the mediastinum with sampling of suspicious lymph nodes prior to attempting a curative surgical approach.

The following criteria are considered when deciding for or against Pancoast tumor resection with spine involvement:

- Histological diagnosis
- Whether the tumor is attached to the vertebral column (demonstrated by radiographic findings)
- Presence or absence of mediastinal nodal involvement
- Presence or absence of distant metastasis

Prognostic factors that predict a poor prognosis have been identified and include direct extension of the tumor into the vertebral bodies, great vessels, brachial plexus, and neck base, involvement of mediastinal (N2, N3) lymph nodes, and incomplete resection with positive margins. However, survival is associated with complete resection, which is a fact that has triggered the search for new treatment modalities.

With the introduction of modern spine reconstruction techniques, some recently published series have stressed the benefit of en bloc resection of locally advanced tumors with vertebral and subsequent spine reconstruction. Two major strategies exist in the treatment of tumors invading the spine, including intraslesional tumor resection with subsequent spine reconstruction, and en bloc resection of the tumor and subsequent spine reconstruction. Although the first strategy is palliative, the second strategy is intended to be curative. Specifically, it is necessary to resect the tumor as 1 piece, without violating the tumor borders, in particular, to strive for the histological proof of tumor-free margins.

In certain cases in which the tumor is in the epidural space, true en bloc resection is impossible. In such cases, the resection is termed “en bloc with planned transgression” and may include the involved dura.

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Current techniques for mediastinal lymph node sampling include endobronchial ultrasonography–guided needle biopsy, transesophageal endoscopic ultrasonography–guided needle biopsy, or mediastinoscopy. If mediastinal N2 or N3 nodes are proven to be invaded by tumor, then patients should be medically treated with chemotherapy and radiation therapy. However, hilar N1 lymph node involvement alone does not preclude surgery, and patients with T3N1 or T4N1 tumors are eligible for the trimodality approach with curative intent.

Because the presence of distant metastases is important when selecting patients with Pancoast tumors, a thorough search for distant metastatic spread begins with an analysis of the patient's history, findings on physical examination, and the results of blood tests. PET/CT plays a critical role in searching for common sites of extracranial metastatic disease. Due to the elevated incidence of brain metastases in locally advanced lung cancer, contrast-enhanced MRI of the brain is recommended to complete the metastatic workup.

CT scans of the chest generally provide information concerning the extent of the Pancoast tumor, including the extent of parenchymal disease along with chest wall and mediastinal lymph node involvement. However, MRI scans are superior to CT scans in terms of imaging tumor extension to the brachial plexus, subclavian vessels, vertebral bodies, and the spinal canal. With the current accuracy of contrast-enhanced CT and MRI scans, in questionable cases venous or arterial angiography is rarely needed to determine whether subclavian vessels are invaded by tumor.
Cytologic analysis of expectorated sputum generally yields a malignant diagnosis in 11% to 20% of cases when the tumor is centrally located, but the yield is much lower with more peripheral tumors. Fiberoptic bronchoscopy with transbronchial biopsy and lavage with cytologic analysis may increase the diagnostic accuracy to 30% or 40%, even in peripheral tumors. However, in the usual peripheral Pancoast tumor, transthoracic CT–guided needle biopsy may be needed to histologically confirm the diagnosis of cancer prior to beginning induction therapy.

**Preoperative Radiation Therapy and Chemotherapy**

The potential benefits of preoperative radiation therapy were first promoted by Shaw et al and include a decrease in tumor size, improved resectability, and a reduction in viable cells, theoretically preventing the dissemination of the tumor during surgery. In addition, by examining the specimen the pathologist may determine whether the irradiation significantly affected the tumor.

The disadvantages of induction radiation therapy include difficulty in determining “true” margins during surgery, because postradiation scarring limits useful, tactile, surgical feedback and visual cues with regard to the limit of the tumor. In addition, complications, such as infection, cerebrospinal fluid (CSF) leakage, pseudarthrosis, and hardware failure, increase with preoperative irradiation. Other disadvantages of preoperative radiation therapy include the symptomatic debilitation of patients before undergoing a major surgical procedure and potential wound-healing problems in which the surgical incision (superior–posterior extent) is located in the radiation field.

The addition of concurrent chemotherapy to preoperative radiation therapy is motivated by the rationale of improving resection rates and preventing or treating occult systemic disease. This approach has proved beneficial as preoperative neoadjuvant therapy in the treatment of high-grade sarcomas; however, the optimum neoadjuvant regimen for Pancoast tumors remains to be determined. The only major multi-institutional phase 2 trial of combined preoperative concurrent and induction chemotherapy with radiation therapy in Pancoast tumors showed a complete resection rate of 92% and a significantly improved survival rate compared with historical control trials of preoperative radiation therapy alone followed by surgery. However, this preoperative regimen is difficult to tolerate because patients with Pancoast tumor often are debilitated, as indicated by the 75% rate of patients in the trial being strong enough to undergo subsequent surgical resection following initial treatment.

Another treatment approach includes high-dose 3-dimensional radiation therapy (dose range, 50–70 Gy) integrated into trimodality therapy by Kwong et al. These investigators recommend performing restaging mediastinoscopy following induction therapy with chemotherapy and radiation therapy, and, if nodes are positive, surgical options should be reassessed in terms of palliation of local symptoms rather than curative surgery. Despite the widespread use of preoperative chemotherapy and radiation therapy for Pancoast tumors, no randomized trials support this treatment, and the paucity of cases with this presentation will likely limit completion of subsequent randomized studies.

Despite the popularity of induction and concurrent chemotherapy with radiation therapy, the recommended dose of induction radiation therapy is 45 Gy, which is minimally cytotoxic for lung cancer. If positive margins are present after subsequent surgical resection, then adding 20 Gy of postoperative radiation therapy (split-course radiation) will have little additional effect. An empirical approach favored by some major cancer centers is induction doublet chemotherapy alone followed 3 to 5 weeks later by resection, and then full-dose postoperative radiation therapy (65–70 Gy), which is a more cytotoxic dose likely to cover close or positive margins. With this approach, we have found no impaired resectability, and patients have a better clinical status prior to surgery and after chemotherapy alone compared with concurrent chemotherapy with radiation therapy. Although this approach has not yet been validated in clinical trials, we estimate that local recurrence rates will be lower than the reported local recurrence rates of 25% to 27.7% for induction and concurrent chemotherapy with radiation therapy.

**Surgical Approaches**

Various surgical approaches have been described for invasive Pancoast tumors with spine involvement requiring vertebral body resection. Recent studies of surgical case series have shown that the use of extended operations to achieve complete resection of locally advanced T4 Pancoast tumors invading the subclavian vessels or spinal column is feasible. The surgical goal is resection of the upper lobe with the involved ribs, transverse processes, and all involved structures (eg, lower trunk of the brachial plexus [T1 nerve root], stellate ganglion, spinal elements) in an en bloc fashion to obtain negative margins.

More advanced T4 tumors are generally resected in 2 stages because instrumentation and spinal stabilization are required. In some studies, a single lateral approach is used for resection and instrumentation placement; however, performing dorsal spinal fixation is technically demanding while maintaining proper alignment with the patient in a lateral position. In the event that instrumentation is not necessary (no verte-
bral body involvement, only chest wall involvement), single-stage surgery through posterolateral thoracotomy (classic Shaw-Paulson approach) may suffice. One alternative approach occasionally favored is the anterior transcervical approach popularized by Dart-evelle et al. This method allows better exposure of the extreme anterior apex of the lung and cervically based structures (brachial plexus and subclavian vessels). The incision parallels the lower border of the sternocleidomastoid muscle and courses across the manubrium, laterally turning below the ipsilateral clavicle.

Grunenwald and Spaggiari developed a transmanubrial technique involving a manubrial L-shaped transection and first costal cartilage resection. Dart-evelle, Fadel et al, and Grunenwald et al developed a combination transcervical or transmanubrial technique and a posterior midline approach.

The trapdoor approach described by Nazzaro et al is often used for an anteriorly located tumor or a tumor mass with kyphotic angulation and/or involvement of the esophagus or the subclavian artery. Although the anterior weight-bearing spinal column can be reconstructed with polymethyl methacrylate, bone graft, or mesh following vertebral body removal, the placement of adequate anterior instrumentation is difficult to achieve using such an approach. Whenever possible, lobectomy is favored for pulmonary resection (with lower recurrence rates than apical segmentectomy); however, in these anterior apical approaches, apical segmentectomy may be substituted, especially for small tumors, with an anticipated good outcome.

Most described surgical methods for locally advanced T4 lesions involve at least 2 stages (tumor types B and C). Typically, spinal stabilization is performed through a posterior approach (first stage) followed by posterolateral or trapdoor thoracotomy for definitive resection (second stage). Our group showed that a single-stage posterior approach is feasible in selected patients and can lead to a good outcome in patients with Pancoast tumors who require spinal stabilization and en bloc resection. Such an approach offers 1-stage definitive resection, spinal stabilization (anterior, posterior, or both), and simultaneous chest wall and lobectomy resection. The surgery is well tolerated when performed in experienced centers, and it eliminates the need for patients to undergo a second-stage operation. However, the thoracic surgeon must perform upper lobectomy through the chest wall defect after the tumor is disconnected from the chest wall and spine, a technique that may be challenging depending on tumor size.

The choice of approach depends on several factors, including the medical and neurological status of the patient; the nature, location, and extent of the tumor; the need for spinal stabilization; and the experience of the surgeons and anesthesiologists. In general, 3 types of spine tumor involvement have been identified. To select the appropriate approach, Pancoast tumors with spine involvement are classified according to the extent of vertebral involvement.

In type A tumors, the chest wall, including the ribs and transverse processes, are involved and instrumentation is not required; therefore, these tumors can be approached and resected by single-stage posterolateral thoracotomy. Scoliosis (nondebilitating) may develop following surgery.

In cases of type B tumors, part of the vertebral body has been infiltrated but is confined to a single side. In such cases, osteotomy is required through the medial wall of the involved pedicle obliquely, followed by an incision through the vertebral body (partial vertebrectomy), combined with posterior instrumentation and fusion. Anterior reconstruction is not necessary because at least 50% of the vertebral body will remain intact. This procedure can be achieved by an initial posterior midline approach with posterior instrumentation, followed later by a definitive resection during second-stage posterolateral thoracotomy.

Type C tumors cross over the midline, involving more than 50% of the vertebral body, thus necessitating anterior reconstruction with a cage, allograft, or polymethyl methacrylate and additional posterior instrumentation in a second-stage procedure through a ventral approach. In such cases, bilateral nerve root clipping is carried out, and osteotomy is performed from the opposite side (total vertebrectomy). This technique can also be carried out as a 2-stage surgical approach, namely, as posterolateral thoracotomy and a posterior midline approach.

As mentioned previously, it is possible to achieve en bloc resection in selected cases with circumferential stabilization in a single-stage, posterior midline approach. An anterior trapdoor approach may be employed when the tumor invades the subclavian artery, esophagus, sternum, and anterior mediastinum. This surgical technique provides exposure in selected cases.

**Surgical Results**

Several surgical series on locally advanced Pancoast tumors suggest that en bloc resection with tumor-free margins results in prolonged rates of survival and an increased median time to recurrence. The rates of complete tumor resections ranged from 56% to 79% compared with rates of 21% to 44% for incomplete resections. Some investigators found a significant difference in rates of median survival times between complete and incomplete resection groups. With complete resection, 2-year survival rates ranged from 47% to 54%, and 5-year survival rates ranged from 14% to 27%. Recurrence rates were 41% to 59%.
Complications

Pancoast tumor surgery involves complications and adverse events related to the need for en bloc resection and the frequent sacrifice of the T1 nerve root and stellate ganglion. Although T1 is not the dominant root innervating the intrinsic muscles of the hand (C8), its sacrifice may lead to hand weakness. However, patients can typically continue to use their hands for daily activities but not for heavy labor. Generally, Horner’s syndrome presents as an aesthetic-related issue rather than a functional one.

Some atrophy of the muscles in the back, along with prominence of the posterior hardware, can be expected. Ipsilateral shoulder misuse due to pain issues can occur, and early physical therapy is instrumental in recovery.

Pulmonary complications (atelectasis and pneumonia) can arise and should be treated with aggressive pulmonary hygiene, careful pain management, and other appropriate interventions. Patients with type A tumors undergoing chest wall resection may develop compensatory scoliosis over time, but this is typically not disabling.

As with any surgical procedure, appropriate planning may prevent most complications. Preoperatively, the number of vertebrae involved must be assessed, as well as the extent of osteotomies and the relationship of the tumor to the subclavian vessels. If the subclavian vessel appears to be involved by tumor, then a vascular surgeon must be involved early on in the planning and execution of the surgical procedure.

The extent and type of instrumentation must also be determined. Hardware failure can occur, including junctional kyphosis/scoliosis, rod breakage (typically at transition points), and pulling out of screws or hooks. Late failures are typically the result of pseudarthrosis and require fusion revision.

Among reported series on surgical treatment of locally advanced Pancoast tumors, mortality rates ranged from 0% to 5%, and complication rates ranged from 28% to 52%.15,16,19,33 The most frequent complications in these series were the result of pulmonary issues such as prolonged intubation for respiratory failure, pneumonia, and atelectasis.

Other complications may include deep venous thrombosis, pulmonary embolism, chylothorax, excessive blood loss, wound dehiscence or infection (particularly in combination with postoperative radiation), nerve root injury, spinal cord injury, injury of the dura with neurological deficits, and CSF leakage. If there is a CSF leak within the thoracic cavity, then treatment may be difficult due to negative intrathoracic pressure. In our experience, this complication typically requires surgical repair with a multilayered patch and a vascularized graft (intercostal muscle or trapezius muscle flap).4

Conclusions

Although no level 1 studies exist on the treatment of Pancoast tumors, the present review provides evidence that triple modality therapy along with complete resection of locally advanced T4 Pancoast tumors with involvement of the spine offers an advantage to other therapeutic modalities or therapies with incomplete resections. Evidence from the literature is insufficient to support the hypothesis that triple modality therapy is superior to other therapeutic modalities in terms of complication rates.

References