Clinical and Surgical Staging of Non-Small Cell Lung Cancer*

Jean Deslauriers, MD, and Jocelyn Grégoire, MD

The necessity for a compulsive attitude toward preoperative assessment of lung cancer is to be emphasized, since rational treatment and prognosis depend largely on the stage of disease at the time of diagnosis. In the preoperative setting, the techniques used should be sequential, logical, and help to identify patients suitable for treatment with curative intent. With regard to the primary tumor (T status), the accuracy of CT or MRI to predict the need for extended resections is limited. Similarly, all noninvasive methods to determine the nodal status (N) are valuable, but mediastinoscopy has a greater sensitivity and specificity than either CT or MRI. The role of routine organ screening for the detection of distant occult metastasis in the asymptomatic patient is still controversial. Ultimately, the prognosis of the resected patient with lung cancer is based on complete intraoperative staging, which can be done by either systematic node sampling or complete lymphadenectomy. At present, neither of these techniques has been shown to improve the quality of staging or survival.

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Key words: clinical staging; lung cancer; surgical staging

Abbreviations: NSCLC = non-small cell lung cancer; PET = position emission tomography; VATS = video-assisted thoracoscopic surgery

Recognizing that surgical treatment is still the best method of controlling lung cancer, surgeons want an operation to be performed when the benefits clearly outweigh the possible risks, and when it has been determined that cancer resection is the most appropriate course of management. The necessity for a compulsive attitude toward preoperative assessment is therefore to be emphasized, since rational treatment decisions and ultimate prognosis of patients with lung cancer depend largely on the stage of disease at the time of diagnosis.1,2

Staging is the measurement of the extent of tumor that allows rational grouping of patients with similar disease for prognostic, analytic, or therapeutic purposes. In the preoperative setting, staging will define patients most likely to benefit from pulmonary resection, while ensuring that no individual is denied the chance of curative resection based on radiologic or clinical findings alone.3 It will also help the selection of patients eligible for induction therapy programs. If proper pretreatment staging is accomplished, the rate of exploratory thoracotomy or incomplete resection should not exceed 8 to 10%.

In 1997, a consensus panel of the International Association for the Study of Lung Cancer* made the following recommendations on pretreatment minimal staging for non-small cell lung cancer (NSCLC): (1) any staging protocol should be simple and widely applicable; (2) the staging protocol should be sequential and logical, avoiding unnecessary tests that might prove expensive and invasive; (3) the staging protocol should identify patients suitable for treatment with curative intent; and (4) any staging protocol should be based on the TNM classification. The purpose of this article is to review the role and relative merits of invasive and noninvasive methods utilized in the staging of patients with lung cancer.

Staging System

The Union Internationale Contre le Cancer and American Joint Committee on Cancer have recently established new criteria for the TNM staging of lung cancer, and the prognosis for the various TNM subsets has also been redefined.5 This staging system uses the TNM classification originally described by Denoix,6 where T indicates site and size of the primary tumor, N relates to nodal involvement according to site, and M indicates the presence or absence of distant metastasis (Table 1).

In this revised classification, the descriptors for the TNM classification have generally remained the same as those described in 1986.7 Tumors classified as T3 are neoplasms that have grown beyond the lung parenchyma to involve structures still amenable to resection, while T4 defines those tumors with extensive extrapulmonary extension, usually precluding curative or complete resection. The T4 descriptor also includes tumors with satellite nodules located within the same lobe.8 Satellite nodules located in the ipsilateral nonprimary tumor lobe(s) of the lung are designated M1.

The problem of nonmalignant pleural effusions has not really been solved, because the use of this descriptor when the effusion is nonbloody and not an exudate is left to clinical judgment.5 It implies that when the effusion is an exudate, as is the case in virtually all paraneoplastic effusions, the tumor should be designated as T4. Patients with cytology-positive malignant effusions are also designated as having T4 tumors.

The issue of site as a descriptor of the T status has been partially addressed. Superficial tumors in which the invasive component is limited to the bronchial submucosa are now classified as T1 tumors, even if they are located within the main bronchus or within 2 cm from the carina. That leaves a number of larger invasive tumors that may be T3 by virtue of their location being proximal to a lobar orifice, but are more likely to behave as T1 or T2 tumors. The new TNM classification still does not establish a difference between T3 tumors invading the parietal pleura and T3 tumors invading the ribs or soft tissues of the chest wall.

The classification of regional lymph node stations has not been clarified by Mountain and Dresler,9 who tried to combine the features of the two systems that have been in use for 30 years, the first one based on the work of Naruke and advocated by the American Joint Committee on Cancer,10 and the second being the nodal map pro-

*From the Centre de pneumologie de l’Hôpital Laval, Sainte-Foy, Quebec, Canada. Correspondence to: Jean Deslauriers, MD, Centre de pneumologie de l’Hôpital Laval, 2725 chemin Ste-Foy, Sainte-Foy, Quebec, Canada G1V 4G5
posed by the American Thoracic Society and adopted by the North American Lung Cancer Study Group. In their proposal, all N2 nodes are contained within the mediastinal pleural envelope and are numbered 1 through 9. It is understood, although not clearly stated, that in many cases, the mediastinal pleura reflexion is difficult to identify, even at surgery, so that the distinction between hilar nodes (N1) and low tracheobronchial nodes (N2) may be difficult to make. Anatomically, the pleural envelope begins just proximal to the origin of the upper lobe bronchus, so that all lymph nodes cephalad to this point should be designated as mediastinal.

The issue of Pancoast tumors, where supraclavicular nodes may be involved by direct transpleural seeding through the apical pleura, has not been addressed. If these nodes contain tumor, they are designated as N3 nodes, although they may be the first nodal station involved.

Table 1—TNM Descriptors in Lung Cancer*

<table>
<thead>
<tr>
<th>Classifications</th>
<th>Descriptions</th>
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<tbody>
<tr>
<td>T factor (primary tumor)</td>
<td></td>
</tr>
<tr>
<td>Tis =</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1 =</td>
<td>T1 tumors are ≤ 3 cm in diameter, surrounded entirely by pulmonary parenchyma or intact visceral pleura, and without evidence of invasion proximal to or including a lobar bronchial orifice. Uncommon superficial tumors of any size with its invasive component limited to the bronchial wall are also classified as T1 tumors. Such superficial tumors are defined histopathologically and may be located within the main bronchus or be &lt; 2 cm from the carina.</td>
</tr>
<tr>
<td>T2 =</td>
<td>T2 tumors are &gt; 3 cm in greatest dimension, invade visceral pleura or present with atelectasis or pneumonia extending to the hilum but not involving the entire lung. The proximal extent of the tumor may include the lobal bronchial orifice, bronchus intermedius, or main stem bronchus, but must be &gt; 2 cm from the carina.</td>
</tr>
<tr>
<td>T3 =</td>
<td>Tumor of any size that directly invades any of the following: chest wall (including superior sulcus), diaphragm, mediastinal pleura, pericardium or tumor in the main bronchus &lt; 2 cm distal to the carina, but without involvement of the carina or associated atelectasis or obstructive pneumonitis of the entire lung.</td>
</tr>
<tr>
<td>T4 =</td>
<td>Tumor of any size that directly invade the deep structures of the mediastinum including the heart, great vessels, trachea, esophagus, vertebral body, or carina. It also includes tumors with a malignant pleural or pericardial effusion or with satellite tumor nodule(s) within the ipsilateral primary tumor lobe of the lung.</td>
</tr>
<tr>
<td>N factor (regional lymph nodes)</td>
<td></td>
</tr>
<tr>
<td>N0 =</td>
<td>No regional lymph node metastasis.</td>
</tr>
<tr>
<td>N1 =</td>
<td>Metastasis to ipsilateral peribronchial and/or ipsilateral hilar lymph nodes, and intrapulmonary nodes involved by direct extension of the primary tumor.</td>
</tr>
<tr>
<td>N2 =</td>
<td>Metastasis to ipsilateral mediastinal and/or subcarinal lymph nodes.</td>
</tr>
<tr>
<td>N3 =</td>
<td>Metastasis to contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene or supraclavicular lymph nodes.</td>
</tr>
<tr>
<td>M factor (distal metastasis)</td>
<td></td>
</tr>
<tr>
<td>M0 =</td>
<td>No distant metastasis.</td>
</tr>
<tr>
<td>M1 =</td>
<td>Distant metastasis present.</td>
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The staging system has also been modified to provide greater specificity for identifying patient groups with similar prognosis and treatment options (Table 2). Stage I has been divided into I-a and I-b because the difference in survival rate between the two groups is significant (p < 0.01). Since there was little difference between the cumulative 5-year survival rates for patients with T2N1M0 and T3N0M0 disease, these were regrouped in stage II-b.

Table 2—Revised Stage Grouping of TNM Subsets*

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM Subset</th>
<th>cTNM</th>
<th>pTNM</th>
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<tbody>
<tr>
<td>I-a</td>
<td>T1N0M0</td>
<td>61</td>
<td>67</td>
</tr>
<tr>
<td>I-b</td>
<td>T2N0M0</td>
<td>38</td>
<td>57</td>
</tr>
<tr>
<td>II-a</td>
<td>T1N1M0</td>
<td>34</td>
<td>55</td>
</tr>
<tr>
<td>II-b</td>
<td>T2N1M0</td>
<td>24</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>T3N0M0</td>
<td>22</td>
<td>38</td>
</tr>
<tr>
<td>III-a</td>
<td>T1-3N2M0</td>
<td>13</td>
<td>23</td>
</tr>
<tr>
<td>III-b</td>
<td>T3N1M0</td>
<td>9</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>T4N0-2M0</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>any T any N M1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

* Reprinted with permission from Mountain; cTNM = clinical stage TNM; pTNM = pathologic stage.
Patients with N2 disease remain in stage III-a, and those with T4 tumors are included in stage III-b disease.

The staging process can be broken down into a clinical stage TNM, determined by pretreatment studies and a pathologic stage TNM, which depends on intraoperative maneuvers by the surgeon and postoperative assessment by the pathologist.

Preoperative Diagnosis

Although some surgeons continue to advocate thoracotomy without diagnosis because “you are going to operate anyway,” adequate treatment planning begins with a proper diagnosis of the underlying disease process. This information allows for a clear discussion with the patient as to what will be done at operation, as well as for streamlining the investigation of the lesion. Further, it avoids the reliance on intraoperative frozen section results, which can at times be misleading.

With improved techniques of biopsy often done under CT guidance, and with refinements in the pathologic interpretation of smaller specimens, the diagnosis of lung cancer can be made preoperatively in virtually all patients. Flexible bronchoscopy is reliable in central tumors, which represent about 30% of all lung neoplasms, while percutaneous fine-needle aspiration biopsy can establish the diagnosis in as many as 90 to 95% of peripheral tumors.14,15 It is important to understand that a negative result does not exclude malignancy, especially if the cytologic findings are reported as unsatisfactory or non-specific inflammation.14 In these individuals, repeat biopsy may be of some value.

Clinical Staging of the T Factor

A careful clinical history and physical examination remains a highly cost-effective staging method, especially in higher-stage tumors invading the chest wall, superior sulcus, or mediastinum. Similarly, standard chest radiographs may on occasion provide evidence of chest wall invasion or of pleural effusion. Bronchoscopy should always be done, not only to determine the endobronchial T status of central tumors, but also to rule out synchronous tumors in other parts of the bronchial tree. In addition, bronchoscopy may be helpful to identify possible candidates for sleeve resection of the main bronchus or carina.16 In those patients, the distance of submucosal spread can be estimated by the use of serial biopsies over distances of 1 to 2 cm proximal and distal to the tumor.

In most cases of presumed intrathoracic spread, CT and MRI will improve the preoperative determination of tumor invasion. Even with the use of these imaging modalities, however, the staging of tumors involving the chest wall or mediastinum and that of Pancoast tumors remains difficult.

In patients with lung cancer suspected of direct invasion into the chest wall, one has to try to predict the need for chest wall resection in order to avoid unnecessary extended resections or unneeded violation of tissue planes. In this respect, patients with chest wall pain associated with tumors that abut the pleura, who have a positive isotope bone scan over the tumor area, or who present with a large soft tissue mass are likely to require chest wall resection.

In a prospective study performed in 112 patients to evaluate the diagnostic accuracy of CT criteria in predicting the extent of chest wall invasion by lung cancer, Ratto et al17 showed that obliteration of the extrapleural fat plane and the ratio between tumor-pleura contact and tumor diameter were the only CT variables significantly related to pathologic findings (Table 3). In that study, the surgeon was almost certain that an extrapleural dissection would not violate the cancer plane if both criteria were negative (sensitivity, 97%), but if both criteria suggested chest wall invasion, the surgeon was advised against extrapleural dissection (specificity, 89%). In 1991, Yukoi et al18 studied 30 patients with a peripheral lung cancer abutting the chest wall but without CT signs of true parietal invasion. After the induction of a diagnostic pneumothorax, repeated CT was carried out with a diagnostic accuracy of 100% for predicting chest wall invasion. Despite these results, CT is generally considered inaccurate to predict the need for chest wall resection,19,20 although obliteration of the extrapleural fat plane and costal osteolysis are highly predictive signs of chest wall invasion. CT also has great difficulty in differentiating between visceral and parietal pleura invasion, because peritumoral inflammatory adhesions often simulate true invasion. CT and MRI appear to be equivalent in their ability to demonstrate chest wall invasion, as reported by the Radiology Diagnostic Oncology Group.21 In one retrospective study from Japan,22 chest wall invasion was evaluated with ultrasonography in 19 patients and confirmed at thoracotomy. The sensitivity, specificity, and accuracy of ultrasonography was 100, 98, and 98%, respectively.

MRI is more accurate than CT to evaluate the local invasiveness of superior sulcus tumors,21,23 particularly their extension to the vertebral body, spinal canal, brachial plexus, and subclavian artery. In a prospective and blinded study of 31 patients with superior sulcus tumors, Heelan et al23 demonstrated that thin-section (5 mm) coronal and sagittal images were more accurate than CT scans (94% accuracy with MRI; 63% with CT) in the evaluation of tumor invasion through the superior sulcus. This information is important, because vertebral body, spinal canal, or upper brachial plexus invasion are contraindications to operation for most surgeons. In that study, the improved

Table 3—CT Scan Criteria for Chest Wall Invasion*  

<table>
<thead>
<tr>
<th>Value, %</th>
<th>Obliteration of Extrapleural Fat Plane</th>
<th>Tumor-Pleura Contact/Tumor Diameter (0.9)</th>
</tr>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>83</td>
<td>83</td>
</tr>
<tr>
<td>Specificity</td>
<td>87</td>
<td>80</td>
</tr>
<tr>
<td>Accuracy</td>
<td>86</td>
<td>81</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>80</td>
<td>71</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>91</td>
<td>89</td>
</tr>
</tbody>
</table>

* Reprinted with permission from Ratto et al.17
accuracy of MRI was interpreted as being related to the ability to image the superior sulcus on thin-section coronal and sagittal images. On occasion, ancillary techniques such as subclavian artery angiography may be indicated to rule out local invasion by superior sulcus tumors. Involvement of the subclavian artery is not considered an absolute contraindication to resection, although invasion of its vertebral branch may make the operation more dangerous. We also suggest that all patients with Pancoast tumors have ultrasonography examination of the ipsilateral vertebral branch may make the operation more dangerous. Both CT and MRI can depict gross mediastinal invasion, but both studies are quite poor in their ability to distinguish between tumor abutting the mediastinum vs a tumor truly extending into a mediastinal structure. In the Radiology Diagnostic Oncology Group report, MRI was statistically significantly more accurate than CT to detect mediastinal invasion. In another report, Glazer et al reviewed 80 patients who had indeterminate mediastinal invasion by CT scan. Forty-eight of these masses (60%) were resectable without true invasion of the mediastinum, 18 masses (22%) focally invaded the mediastinum but were still technically resectable, and 14 masses (18%) were unresectable. CT findings considered to be indicative of complete resection included contact of ≤ 3 cm with the mediastinum, < 90% contact with the aorta, and the presence of mediastinal fat between mass and mediastinal structures. Based on these results, one must therefore be very careful before determining that a given tumor is unresectable based on CT criteria alone.

MRI appears to be superior to CT to demonstrate heart and great vessel invasion, while tumors invading to the thoracic aorta may be best shown by cine CT. In some cases of left atrial involvement, transesophageal ultrasonography may also be useful to determine the depth of invasion. In central tumors invading the main pulmonary artery, it is often impossible to determine preoperatively the exact T status (T3 or T4), so that thoracotomy must be done to ascertain tumor resectability.

The parietal pleura can be involved by a direct extension of the tumor or indirectly through subpleural lymphangitic spread or pleural metastasis. While direct invasion is not a major problem, indirect invasion is always a sign of inoperability that must be documented preoperatively. CT is more accurate than standard radiographs to document the presence of small effusions (< 25 mL), and when fluid is present, it is important to determine its true nature. This can be done by thoracentesis, percutaneous pleural biopsy, or video-assisted thoracoscopic surgery (VATS), which allows direct assessment of the pleural surfaces. By VATS examination, Asamura et al were able to demonstrate inoperable factors in 5 of 135 patients with presumed operable lung cancer. Four had a malignant pleural effusion, and one had extensive dissemination without effusion.

**Clinical Staging of the N Factor**

The presence of metastases to regional lymph node significantly influences the treatment and prognosis of patients with NSCLC. The presence of N1 nodes, although rarely of crucial importance except perhaps in patients with T3-T4 tumors, means more extensive resection with increased surgical risk and reduced prospects for cure. At present, the techniques used for preoperative documentation of N1 status are imperfect, and CT does not appear to be better than chest radiographs or oblique tomograms, especially in cases where the hilum is of normal size on routine examination. Hilar abnormalities may be easier to detect with MRI because nodes can be more readily distinguished from local vessels by this technique.

The presence of mediastinal lymph node metastasis (N2, N3 disease) is an ominous prognostic sign; stage III-b disease, by virtue of metastatic contralateral lymph nodes in the mediastinum or hilum, is an absolute contraindication to surgical resection. Physical examination can detect enlarged supraclavicular or scalene nodes, but this type of examination is notoriously inaccurate if done by an inexperienced examiner. Careful clinical-history taking and physical examination can also detect evidence of superior vena cava obstruction or left recurrent nerve palsy, both being nearly absolute signs of N2 disease. Enlarged nodes within the mediastinum on standard radiographs are highly specific, if insensitive, signs of N2 disease.

Advanced invasive and noninvasive techniques are currently used to preoperatively determine the status of mediastinal nodes. Imaging modalities such as CT and MRI can demonstrate nodal enlargement but cannot confirm histologic involvement. On the other hand, more invasive procedures such as mediastinoscopy, anterior mediastinotomy, VATS, and ultimately thoracotomy are more specific in assessing lymph nodes but require operative intervention. At present, the choice of techniques to be used continues to be one of the most controversial issues in the staging of lung cancer.

The major contribution of CT is to allow the surgeon to proceed directly to thoracotomy if the nodes have a transverse diameter of < 1 cm, where the likelihood of finding metastatic tissue is in the range of 3 to 16%. The accuracy improves if the primary tumor is peripheral or of squamous histology, but decreases if the tumor is central or of nonsquamous histology. Lymph nodes that have a diameter of 1 to 2 cm by CT contain metastatic tissue in 70% of cases, while those > 2 cm have an even greater chance of containing tumor tissue. In a meta-analysis of CT accuracy for assessment of mediastinal lymph nodes in lung cancer, the authors reported a sensitivity, specificity, and overall accuracy of 79, 78, and 80%, respectively.

The predictive value and accuracy of CT in determining mediastinal node involvement is lower in the presence of distal obstructive pneumonitis or old granulomatous dis-
ease, and MRI has generally not been shown to be more accurate than CT to evaluate nodal disease.44 For these reasons, there is general agreement that enlarged lymph nodes require histologic confirmation if this finding means inoperability. In other words, suspected inoperability on the basis of abnormal findings from noninvasive procedures should always be confirmed by direct biopsy.

Imaging with whole-body positron emission tomography (PET) appears to be more accurate than CT for the diagnosis of mediastinal node metastasis. In one study carried out in 76 patients,35 mediastinal PET and CT findings were compared with results of surgical staging. Sensitivity and specificity for the diagnosis of N2 disease were 83% and 94% for PET, and 63% and 73% for CT, respectively. PET is also valuable to detect occult adrenal or liver metastases not documented by other means of nonsurgical staging. A recent Technology Evaluation Center of Blue Cross/Blue Shield report36,37 concluded that the literature supported the use of fluorodeoxyglucose-PET for staging lung cancer, even if the technology is currently unavailable in most centers.

Most invasive procedures used to determine the nodal status involve long tubes passed through small holes into highly vascular surroundings.28 Despite this frightening description, these techniques can be carried out with low morbidity if the operator is experienced and familiar with the local anatomy. Perhaps less invasive, needle aspiration biopsy done through a transtracheal or transthoracic approach may be useful to stage patients with inoperable tumors and an enlarged mediastinum on chest radiograph or CT. In 1996, Akamatsu et al39 reported a sensitivity of 88% and specificity of 100% for CT-guided percutaneous cytology of mediastinal lymph nodes. In yet another study, Silvestri et al40 showed that esophageal endoscopic ultrasonography with fine-needle aspiration complemented mediastinoscopy in the assessment of lymph nodes located in the aortopulmonary window or subcarinal space.

As reported by Carlens41 and Pearson et al,42-43 mediastinoscopy involves the inspection, palpation, and biopsy of superior mediastinal lymph nodes. It is a useful and accurate technique that should be used when nodal involvement as determined by CT is unclear (nodes > 1 cm in diameter), or when it is required to have an exact knowledge of mediastinal involvement, such as in higher stage (T2-T3), centrally located, or undifferentiated tumors. In patients where induction treatments are contemplated, mediastinoscopy should be mandatory. Because mediastinoscopy has a greater sensitivity and specificity than CT scanning to document mediastinal node involvement, some centers still recommend its routine use in all presumed operable lung carcinomas.44-45 Ideally, nodes from stations 2, 4, and 10 should be sampled routinely along with the subcarinal (station 7) nodes, as described in the American Thoracic Society staging system.11 Mediastinoscopy may be utilized safely in patients with superior vena cava obstruction and in patients who have had a prior mediastinoscopy. It can be done on an outpatient basis,46 or at the time of thoracotomy.

Lymph nodes located in the aortopulmonary window (station 5) are not accessible by cervical mediastinoscopy, but biopsy can be performed through a left anterior mediastinotomy,47,48 often referred to as a Chamberlain procedure,49 or through an extension of standard cervical mediastinoscopy.50,51 The information gained by these procedures is particularly important for patients with left upper lobe lesions, where survival figures for patients with resectable disease and metastatic subaortic nodes approaches that of patients with N1 disease.52,53 In most centers, these procedures are only done if the aortopulmonary nodes appear to be enlarged on CT scan.

Scalene node biopsy is indicated when they are palpable or in patients who have proven N2 disease prior to undergoing resection. Lee and Ginsberg54 have shown unsuspected microscopic involvement of the scalene nodes in 15% of patients with N2 disease at mediastinoscopy, and in 68% of patients with N3 disease. This information may be relevant in patients for whom an operation is recommended despite N2 disease, or in patients for whom neoadjuvant therapy is considered.

The role of VATS to access mediastinal nodes is unclear,55-57 although nodes located in the aortopulmonary window or posterior mediastinum can be readily obtained by this technique. The potential of VATS to disclose hilar disease may be of importance in patients who cannot tolerate pneumonectomy, or in patients in whom N1 disease may need to be documented histologically prior to induction therapy.

**Clinical Staging of the M Factor**

The most useful assessment of the M factor is done by complete history and physical examination. While significant weight loss and debility are usually symptoms of metastatic disease, focal symptoms, such as headaches or musculoskeletal pain, or abnormal levels of alkaline phosphatase require further investigation. It is of interest to note that patients with brain or bone metastases are often symptomatic, while patients with liver or adrenal metastasis seldom are symptomatic. Whether routine screening for occult metastatic disease is required for every patient with presumed operable lung cancer remains controversial.58,59 In early-stage asymptomatic tumors, the yield of routine organ screening is in the range of 1 to 4%,60-62 and therefore should not be recommended. In one study from the United Kingdom,63 the determination of metastatic disease by CT scanning was addressed in 114 consecutive patients with NSCLC who, on the basis of history, clinical examination, chest radiography, and bronchoscopy, had been considered potentially operable. CT of the abdomen and brain detected occult metastasis in 15 patients (13%), but the extrathoracic abnormality proved to be the only contraindication to surgery in only 3 patients. In potentially operable asymptomatic patients with mediastinal node involvement or with tumors of nonsquamous histology,64 routine multiorgan screening yields a greater number of extrathoracic metastases,61 and may therefore be recommended.65,66

Common sites of distant metastases from lung cancer are the brain (10%), bone (7%), liver (5%), and adrenal glands (3%).67 Focal metastatic nodules in the liver can be detected by contrast-enhanced CT or sonography, with sensitivities in the range of 80%.29,68,69 Histologic confir-
Contrast-enhanced CT and MRI have replaced radio-nuclide scans to detect brain metastasis, with MRI being reserved for patients with high suspicion despite negative CT. Gadolinium-enhanced T1-weighted MRI scans are more sensitive than contrast CT for detecting brain metastasis. In one study, it was concluded that because of expense and lack of positive findings, neither MRI nor CT were indicated in the asymptomatic patient.

Metastatic disease to the adrenals is usually discovered by routine CT scanning of the upper abdomen. A biopsy should be done of unilaterally enlarged glands, because in about 80% of cases, these masses will be benign. Metastatic disease is more likely if the adrenal mass is > 3 cm in diameter, or if the mass alters the usual concave border of the gland. MRI imaging offers no significant advantage over CT, but in one study, the chemical-shift MRI technique was shown to be highly accurate for distinguishing benign from malignant adrenal masses.

Technetium 99m methylene bone scintigraphy is the method of choice to demonstrate skeletal metastasis. Multiple areas of increased uptake have a specificity of 80 to 90% for metastasis. If the presence of metastatic disease remains in question with a positive scan, correlative radiographs or CT should be obtained and, in some cases, CT or sonography-guided percutaneous biopsies should also be done. One of the main values of bone scanning is to provide a baseline, should the patient present with musculoskeletal pain sometime after his operation.

INTRAOPERATIVE STAGING

The ultimate stage of the resected patient depends on accurate intraoperative staging, which can either be done by nonsystematic or systematic lymph node sampling or by complete mediastinal node dissection.

Lymph node sampling in a nonsystematic fashion is inadequate for accurate staging. In an interesting study, Gaer and Goldstraw reviewed 100 thoracotomies done for lung cancer, and compared the naked-eye assessment of nodal staging with the ultimate histologic diagnosis. False-positive assessment was made at 14 node stations (11 patients), and false-negative assessments were made at 10 lymph node stations (9 patients). In that study, the sensitivity, specificity, and overall accuracy of naked-eye assessment was 71.4, 94.4, and 91.6%, respectively.

Whether complete mediastinal node dissection improves the quality of staging and length of survival over systematic sampling remains controversial, even if lower stage tumors are known to have a high incidence of mediastinal node metastases. In a retrospective study of 337 patients with T1 tumors who had undergone pulmonary resection with complete mediastinal lymphadenectomy, Asamura et al showed that 88 patients (26.1%) had lymph node involvement: 32 (9.5%) at N1 nodes, 55 (16.3%) at N2 nodes, and 1 at N3 nodes. The authors concluded that complete hilar mediastinal lymphadenectomy should be routinely done. Ishida et al (Table 4) and Martini et al also concurred that it is important to do a complete mediastinal lymphadenectomy. Ishida et al further documented that for patients with N1 or N2 disease, “skip metastases” are present in > 25% of cases.

Despite these data, most surgeons, including surgeons involved in Lung Cancer Study Group clinical trials, prefer the technique of systematic node sampling, which consists of lymph node biopsy at multiple predetermined levels within the mediastinum and bronchopulmonary areas. This technique is simple, faster, and may involve less morbidity than complete lymphadenectomy. It may, in addition, be just as accurate if mediastinoscopy has been done preoperatively. If the patient is found to have N1 or N2 disease, systematic nodal dissection should be performed.

Two studies compared systematic sampling to mediastinal lymphadenectomy in terms of their ability to stage the mediastinum intraoperatively. In a retrospective study, Bollen et al concluded that the discovery ratio for N2 disease in the mediastinal node dissection and systematic sampling groups were similar, and both were better than nonsystematic sampling. The second study is that of Izbicki et al, who directly compared mediastinal lymph node dissection with systematic sampling in a prospective randomized trial involving 201 patients. These investigators showed that, regardless of the type of lymphadenectomy performed, the percentage of pathologic N1 or N2 disease was very similar in both groups (sampling, 23%, n = 23; lymphadenectomy, 26.8%, n = 22). Lymphadenectomy resulted in a more detailed staging, with detection of significantly more patients with multiple levels of involvement. The role of bilateral mediastinal node dissection remains unclear, although it is unlikely to have a major impact on techniques of resection.

CONCLUSION

Because decision making in managing lung cancer depends more on the clinical stage than on histology of the tumor, the importance of complete preoperative evaluation cannot be overemphasized. This is even more important in the context of pulmonary resection, where morbidity is related to cardiopulmonary events, most of which can also be identified and prevented prior to surgery. Pathologic staging that depends on complete intraoperative sampling not only reflects the ultimate stage of the resected patient but is also indicative of its prognosis.
REFERENCES

6 Denoix PF. Enquête permanente dans les centres anticancéreux. Bull Int Natl Hyg 1946; 1:70–75
36 FDG positron emission tomography for non-CNS cancers. Chicago, IL: Blue Cross/Blue Shield TEC Assessment Program, 1997; 5