Chest CT for Known or Suspected Lung Cancer*

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Lung cancer causes more cancer-related deaths in the United States than any other malignancy. Two facts account for this disturbing observation. The incidence of lung cancer in both men and women has progressively increased in recent years. Treatment of lung cancer remains largely ineffective. The overall 5-year survival rate for patients with lung cancer may be as low as 7 percent to 14 percent. The best survival rates are found in the subgroup of patients with lung cancer with surgically resectable tumors. Clinicians, therefore, are vitally interested in recognizing lung cancer early and determining surgical resectability accurately.

Computed tomography (CT) was introduced into clinical practice in the 1970s as an exciting new method for imaging the thorax. Since then, clinicians have come to rely heavily on CT for evaluating potentially malignant chest lesions and the intrathoracic spread of lung cancer. A survey of thoracic surgeons in 1986 revealed that more than one third of these surgeons order CT routinely for all patients with lung cancer and 62 percent more selectively obtain CT scans.1 Despite the frequency at which clinicians obtain CT scans, it is still unclear what role CT plays in the treatment of patients with suspected and known lung cancers. Clinicians are especially concerned with how well CT performs in distinguishing benign from malignant solitary pulmonary nodules (SPN) and in staging the primary tumor (T) and regional node (N) extent of lung cancer (Table 1). In this review, the role CT should play in evaluating SPNs and assessing the T and N stages of lung cancer will be critically evaluated.

Distinguishing Benign From Malignant Nodules

An appealing way to distinguish between benign and malignant SPNs would be to rely on some combination of radiographic features seen on either the

<table>
<thead>
<tr>
<th>Stage and Node</th>
<th>CT Role Evaluated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumor stage Tx or Tis</td>
<td>No! by definition</td>
</tr>
<tr>
<td>Tumor not radiographically detected</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Yes for invasion and also to distinguish benign from malignant nodules</td>
</tr>
<tr>
<td>A tumor (\leq 3 \text{ cm} ) in greatest dimension without local or proximal bronchus invasion</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>Yes for invasion and bronchial spread</td>
</tr>
<tr>
<td>A tumor (&gt;3 \text{ cm} ) in greatest dimension or with visceral pleura invasion or associated atelectasis/obstructive pneumonitis</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>Yes for invasion</td>
</tr>
<tr>
<td>A tumor invading chest wall, diaphragm, or mediastinal pleura or pericardium</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>Yes for invasion but no for malignant effusion</td>
</tr>
<tr>
<td>A tumor involving heart, great vessels, trachea, esophagus, vertebral bodies, or carura; or with malignant effusion</td>
<td></td>
</tr>
</tbody>
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Node involvement by tumor

<table>
<thead>
<tr>
<th>Node involvement by tumor</th>
<th>CT Role Evaluated</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>Yes</td>
</tr>
<tr>
<td>No regional nodes involved</td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>Not emphasized</td>
</tr>
<tr>
<td>Ipsilateral hilar nodes only</td>
<td></td>
</tr>
<tr>
<td>N2</td>
<td>Yes</td>
</tr>
<tr>
<td>Ipsilateral mediastinal and/or subcarinal nodes</td>
<td></td>
</tr>
<tr>
<td>N3</td>
<td>Yes</td>
</tr>
<tr>
<td>Contralateral mediastinal, hilar, scalene, and/or supraclavicular nodes; ipsilateral, scalene, and/or supraclavicular nodes</td>
<td></td>
</tr>
</tbody>
</table>

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standard frontal and lateral chest radiograph (CXR) or linear tomography. Although there are no classic radiographic features of lung cancer, size is an obvious consideration. Nodules smaller than 8 mm are usually considered benign, and nodules larger than 3 cm are more often malignant. There are other radiographic features strongly suggesting the benign nature of an SPN. The most reliable of these radiographic features seem to be documented absence of growth of the SPN over a 2-year period and substantial calcification in either a central, diffuse, laminated, or popcorn pattern. Other variables considered include nodule shape, edge definition, satellite lesions, and cavitation. Unfortunately, evaluation of these radiographic features on standard roentgenograms may often be subjective. In 1980, Siegelman et al\(^2\) suggested that CT could be used to distinguish between benign and malignant nodules in a quantitative fashion. Because CT is more sensitive than standard radiographic techniques in detecting calcification and the extent of calcification found on CT can be expressed quantitatively as a density, Siegelman's group postulated that an SPN with density numbers suggesting extensive calcification would be most probably benign. The nodules they studied that were dense (>164 Hounsfield units) did indeed prove to be benign.\(^2\) Others found similar results.

Soon after these promising initial reports, the reproducibility of densitometry results was questioned. A variety of technical and geometric variables were found to preclude obtaining consistent CT densitometry results not only in different CT machines, but even with the same CT machine repeatedly over time. The major technical variables affecting CT densitometry are the CT algorithm used to reconstruct the CT density distribution, slice thickness, and kilovoltage. There are also geometric variables related to the patient, such as patient size, nodule size, nodule position in the thorax, and tissue density surrounding the nodule. Concern over standardization issues led Zerhouni and colleagues\(^3\) to develop a reference phantom for quantitative analysis of SPNs. This phantom would serve as a calibration standard for either different CT machines or the same CT machine over time. A nodule density higher than that of the phantom would suggest malignancy.

Numerous studies have described the ability of CT densitometry to identify nodules that are most probably benign (Table 2). In interpreting the results of these studies, several important points concerning CT densitometry have to be considered. First, as discussed by Swensen et al,\(^4\) a suitable density for the standard phantom has not been established. The phantom nodule used in the original multicenter study evaluating its effectiveness was equivalent to 264 Hounsfield units,\(^5\) a value considerably higher than that used in earlier studies. The reason for choosing this density was to minimize misdiagnosis of malignant lesions as benign. However, later studies probably used phantoms with considerably lower reference densities. To ensure uniform acceptance of a standard phantom, its density must be established in a nonarbitrary fashion. Second, SPNs with a density lower than that of the reference phantom were classified as indeterminate because of the extensive overlap between benign and malignant nodule densities in this range. A substantial number of benign nodules have low densities (Table 2). Third, there are numerous methodologic limitations in these studies. Different machines were used among studies. Often, different CT machines were used in the same study, presumably reflecting the introduction of more sophisticated equipment over time. Techniques for performing CT studies, especially slice thickness, often varied. It is not clear that CT scan thickness was appropriately adjusted for nodule diameter in these studies. It is also not clear whether use of the phantom could accommodate all of these variations. Fourth, the nature of the SPNs was not always verified histologically and clinical follow-up varied.

### Table 2—Studies Using CT Densitometry to Evaluate Solitary Pulmonary Nodules

<table>
<thead>
<tr>
<th>Source, yr</th>
<th>Reference Density (HU)*</th>
<th>Nodules Denser Than Reference</th>
<th>Nodules Less Dense Than Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siegelman et al,(^2) 1980</td>
<td>164</td>
<td>20 Benign</td>
<td>58 Malignant 13 Benign</td>
</tr>
<tr>
<td>Godwin, 1982(^1)</td>
<td>165</td>
<td>6 Benign</td>
<td>14 Malignant 16 Benign</td>
</tr>
<tr>
<td>Zerhouni et al,(^3) 1983</td>
<td>164</td>
<td>11 Benign</td>
<td>24 Malignant 6 Benign</td>
</tr>
<tr>
<td>Proto, 1985(^1)</td>
<td>200</td>
<td>44 Benign</td>
<td>96 Malignant 37 Benign</td>
</tr>
<tr>
<td>Jones, 1989(^1)</td>
<td>185</td>
<td>10 Benign</td>
<td>9 Malignant 11 Benign</td>
</tr>
<tr>
<td>Ward, 1989(^1)</td>
<td>...(^1)</td>
<td>20 Benign</td>
<td>17 Malignant 13 Benign</td>
</tr>
<tr>
<td>Houston, 1989(^1)</td>
<td>...(^1)</td>
<td>32 Benign</td>
<td>26 Malignant 33 Benign</td>
</tr>
<tr>
<td></td>
<td></td>
<td>143 Benign</td>
<td>244 Malignant 149 Benign</td>
</tr>
</tbody>
</table>

*HU=Hounsfield units.


\(^2\)Reference phantom density not clearly stated.
Fifth, selection criteria for which patients were included in the studies were not always made clear. Screening studies, such as fluoroscopy and linear tomography, were often used to select patients for CT densitometry.

Although the phantom was an exciting technological step forward for CT, radiologists quickly became skeptical of its value. In a large multicenter study evaluating the phantom, the authors stated that "interpretation of thin section CT scans cannot be purely quantitative, and no immutable CT number can be defined to distinguish benign from malignant nodules." As a consequence of this hesitancy to rely solely on densitometry, radiologists have evolved a hybrid approach, using both quantitative and qualitative features of the CT scan, to distinguish benign from possibly malignant SPNs. The quantitative feature is comparison of the nodule density with that of the reference phantom. The qualitative aspects of CT have been adapted from earlier work with standard radiographs and linear tomography. Because CT can more accurately visualize the SPN than either of these two radiographic techniques, it allows better assessment of the size, shape, edge definitions, and internal characteristics of the SPN. Siegelman's group\(^6\) was the first to incorporate qualitative features of the SPN, determined by thin-section high-resolution CT (HRCT), into criteria also including CT densitometry for identifying benign nodules. The key features used by this group were maximal diameter of the SPN, margin characteristics, distribution and extent of nodule calcification, and presence of fat within the nodule. Other groups used a similar approach (Table 3).

It appears that both techniques, CT densitometry alone and the hybrid approach incorporating thin-section HRCT to qualitatively assess the SPN and the CT reference phantom to quantitatively measure density, are quite accurate in labeling SPNs as benign. With CT densitometry alone (Table 2), only two malignant nodules were misclassified as benign out of a total group of 145 benign nodules (1.4 percent). The hybrid approach (Table 3) misclassified 12 malignancies as benign out of 359 (3.3 percent). Current radiologic practice has evolved to accept the high likelihood that these CT techniques accurately identify benign SPNs. Radiologists may suggest that biopsy and surgical intervention be avoided in these CT-identified benign nodules while growth characteristics are assessed over time (the wait-and-watch strategy). In a small number of cases, CT may establish a benign diagnosis, eg, round atelectasis, arterial-venous malformation, hamartoma, etc, with certainty.

The appropriateness of the wait-and-watch approach to CT-identified benign SPNs, intuitively advocated by radiologists, has been supported by mathematical modeling techniques. Kunstaetter et al\(^7\) and Cummings and colleagues\(^8\) used decision analysis to compare three different strategies, wait-

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**Table 3—Studies Using Thin-Section High-Resolution CT and CT Densitometry to Evaluate Solitary Pulmonary Nodules**

<table>
<thead>
<tr>
<th>Source, yr</th>
<th>Size, cm</th>
<th>Margins</th>
<th>Calcification</th>
<th>Characteristics</th>
<th>Density (HU)*</th>
<th>Benign</th>
<th>Indeterminant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siegelman et al,(^6) 1986</td>
<td>&lt;2.5</td>
<td>smooth or lobulated</td>
<td>High attenuation values</td>
<td>Fat</td>
<td>164</td>
<td>176 Benign</td>
<td>355 Malignant</td>
</tr>
<tr>
<td>Zerhouni et al,(^5) 1986</td>
<td>&lt;3.0</td>
<td>smooth or lobulated</td>
<td>Central with &gt;10% cross-sectional area calcified</td>
<td>...</td>
<td>264</td>
<td>65 Benign</td>
<td>176 Malignant</td>
</tr>
<tr>
<td>Swensen et al,(^4) 1992</td>
<td>&lt;3.0</td>
<td>smooth or lobulated</td>
<td>Central, diffuse, or laminated with &gt;10% cross-sectional area calcified</td>
<td>...</td>
<td>185</td>
<td>75 Benign</td>
<td>10 Malignant</td>
</tr>
<tr>
<td>Khan et al,(^1) 1991</td>
<td>&lt;3.0</td>
<td>smooth or lobulated</td>
<td>Diffuse, central, fat laminated, or popcorn with &gt;10% cross-sectional area calcified</td>
<td>...</td>
<td>...</td>
<td>31 Benign</td>
<td>7 Malignant</td>
</tr>
</tbody>
</table>

\(^*\)HU=Hounsfield Units.


\(^\dagger\)Not clearly stated.
and-watch, biopsy by either transtracheal needle aspiration or fiberoptic bronchoscopy, and immediate surgery, for managing a SPN. In both analyses, if the probability of malignancy were below 3 percent, the wait-and-watch strategy provided the longest calculated life expectancy. Nodules identified as benign by CT densitometry or the hybrid approach have a probability of malignancy in this range.

Although CT techniques seem to be effective in accurately identifying benign SPNs, they are not as reliable in identifying malignant SPNs. Nodules that do not meet the criteria for benignity are classified as indeterminant. Indeterminant nodules are more frequently malignant, but a substantial number are benign (Tables 2 and 3). Decision analysis studies indicate that the immediate surgery option yields the highest calculated life expectancies only if the probability of malignancy is quite high, possibly above 85 percent. The published studies do not clearly show that an indeterminant diagnosis from CT provides an estimated probability of malignancy high enough to support following this option. More recent work, however, suggests that malignancy can be ascertained from CT with a greater degree of certainty by more careful attention to the internal characteristics of the SPN, axial multiplanar reconstruction of CT studies to assess the relationship of the SPN to pulmonary veins, evaluation of the SPN contrast enhancement, and presence of an air bronchogram within the nodule. Another possible method for more accurately identifying malignant SPNs is to incorporate CT features and clinical parameters into formulas based on Bayes' theorem. Cummings et al advocated the use of the likelihood ratio form of Bayes' theorem, using such simple clinical variables as patient age and smoking history, to estimate the probability of malignancy in an SPN. The only radiologic parameter used in this study was diameter of the SPN. More recent studies using this type of mathematical approach have increased the number of clinical and radiologic variables used in their calculations and have substantially improved their accuracy rate in distinguishing benign from malignant SPNs. Results from CT were considered, but apparently thin-section HRCT and CT densitometry were included only infrequently.

Even though thin-section HRCT and CT densitometry are helpful in more clearly identifying a small group of SPNs as highly likely to be benign, clinicians should still be cautious in applying this information to an individual patient. Decision analysis studies suggest that the degree of certainty provided by a benign CT diagnosis is sufficient to favor a wait-and-watch approach to the nodule, but the benefit is only marginal, a few days difference in calculated life expectancy compared with more aggressive strategies. When different management strategies result in such similar calculated outcomes, patient preference becomes critical in choosing a course of action. Furthermore, even if a wait-and-watch approach is adopted, it still mandates careful periodic reassessment of the SPN.

An unresolved question is whether and/or how CT should be integrated into an overall strategy for evaluating SPNs. Special CT techniques should not be routinely used in the initial assessment of an SPN. With most nodules, management decisions can be made reasonably from information provided by standard radiographic techniques and the clinical history. Assessment from standard radiographs of growth rate, calcification, and edge margins should be the first diagnostic step. If the standard CXR or linear tomography shows either absence of growth for more than 2 years or dense, diffuse, central, laminated, or popcorn calcification, the nodule can safely be considered benign without CT. Alternatively, if these radiographic techniques show that the nodule has a spiculated edge or cavitation, it should be considered indeterminant without CT. Reasonable estimates of the probability of malignancy in a nodule may also be obtained by using derivations of Bayes' theorem and clinical and standard radiographic findings.

It is unclear from the available literature how large a subgroup of SPNs cannot be managed with the above approach. If CT were to be included as another intermediate diagnostic test before biopsy, the medical community should be reassured that this would be a cost-effective approach. There are several reasons suggesting that CT for SPNs may not be cost-effective. Special CT techniques may be expensive. Thin-section HRCT and CT densitometry can generally classify only a small proportion of SPNs, probably less than a third, as benign. Even in these nodules with a very high probability of benignity, the estimated survival advantage for the wait-and-watch approach seems to be small.

A parallel concern for clinicians evaluating an SPN is whether CT should be used to detect other parenchymal nodules. It is clear that CT is more sensitive than standard tomography for detecting nodules. Mitchell et al reviewed the CT scans of a large heterogenous group of patients with proven lung cancer and found that more than a quarter of these scans revealed nodules not seen on standard CXRs. There is reasonable information available, however, indicating that CT in a patient with an SPN will only rarely detect additional nodules. Multiple primary lung carcinomas are rare. A recent study showed that CT revealed no additional nodules in a group of 36 patients with T1, N0, M0 disease. Kunio and colleagues reviewed the records of 701 consecutive
patients who underwent surgical resection of lung cancer. Only three patients in this group had additional parenchymal lesions detected by preoperative CT.11

In summary, management decisions regarding most SPNs can be made reasonably using information obtained from the clinical evaluation and standard CXR techniques. Special CT procedures should be reserved for the occasional patient with either equivocal or lacking data and in whom further evidence favoring benignity for the SPN would alter the clinical approach. Routine use of CT to screen patients with SPNs for additional parenchymal nodules is not appropriate.

IDENTIFYING ENDOBRONCHIAL ABNORMALITIES

Thin-section HRCT has proved to be a useful method for visualizing the bronchial tree. In normal subjects, most segmental bronchi and even subsegmental bronchi can be seen quite well. The lingular bronchi are probably the most difficult to identify consistently. These encouraging findings led Naidich and colleagues12 and others to apply CT to evaluate abnormalities of the bronchial tree in various disease states, eg, bronchogenic carcinoma, adenoma, tuberculous bronchial stenosis, hemoptysis, and atelectasis. Because CT performed well in identifying bronchial tree abnormalities in these preliminary studies, several groups directly compared CT with fiberoptic bronchoscopy (FOB) for detecting bronchial involvement in lung cancer. Although Colice et al13 reported only moderate sensitivity and specificity for CT, others showed that CT had similar accuracy to FOB in identifying sites of bronchial involvement by lung cancer.

A safe, convenient, and accurate noninvasive technique for evaluating the bronchial tree, such as CT, might provide benefits for the clinician managing lung cancer in three separate ways. First, lung cancer staging requires an assessment of bronchial tree involvement. Submucosal spread of tumor along the proximal airways or unsuspected contralateral endobronchial disease in most cases precludes surgical resection of the primary tumor. Little information is available on how well CT performs in outlining the submucosal proximal extent of disease spread. A disturbing observation has been that biopsy of a carina appearing normal to the bronchoscopist may yield submucosal tumor in a small percentage of patients with lung cancer. It is not clear that CT would be able to detect such an abnormality. Rarely, contralateral endobronchial disease may occur and may be missed by CT.13

Second, specialized treatment modalities for lung cancer require careful evaluation of the bronchial tree. Computed tomography undoubtedly plays an important role in assisting the surgeon in planning tracheal and/or bronchial reconstruction procedures during lung cancer resection. Several groups have also shown that CT plays a valuable adjunctive role to bronchoscopy in planning laser photoresection of endobronchial tumor. The major advantages of CT over FOB are its ability to image the extraluminal components of the tumor and the bronchial tree distal to an area of airway obstruction.

Finally, CT may play a role in determining the appropriate approach to taking a biopsy specimen from an SPN. Decision analysis studies suggest that SPNs judged to be indeterminant in nature, ie, neither clearly malignant nor clearly benign, should have biopsy specimens taken before definitive treatment decisions are made. Unfortunately, these studies did not compare the efficacy of the two approaches generally used to obtain tissue or cytology specimens from SPNs, FOB, and transthoracic needle aspiration.
Bronchus either leading to or contained within a nodule or mass (Fig 1), which is seen in nodules more readily identifiable by FOB. When the bronchus sign is not found, the diagnostic rate for FOB for these SPNs falls from 60 percent to 30 percent.\(^8\) Gaeta et al\(^{15,16}\) reported similar findings. A diagnostic rate this low for FOB is disheartening and Naidich et al\(^{14}\) and Gaeta et al\(^{15,16}\) have urged that TTNA be used preferentially in cases where a bronchus sign is not identified on CT.

From a bronchoscopist’s viewpoint, the relationship between a positive bronchus sign on CT and improved diagnostic yield from FOB is intuitively obvious. Considerable information is available showing that the diagnostic yield from FOB is higher when tumor is visible at bronchoscopy. A positive bronchus sign is usually seen in central tumors that would more likely be bronchoscopically visible.\(^{14}\) It should also be appreciated that bronchoscopists can use innovative techniques to improve the FOB diagnostic yield for tumors not visible at bronchoscopy. Transbronchial needle aspiration and selective bronchial lavage are both useful methods for diagnosing peripheral lung cancers. Ono et al\(^{17}\) reported a remarkable 98 percent FOB diagnostic yield for small peripheral carcinomas when bronchoscopy and curet biopsy were used.

In summary, CT appears to be a useful method for visualizing the bronchial tree, but its role in staging the endobronchial spread of lung cancer is not clear at present. Computed tomography seems to be very helpful for the surgeon and laser bronchoscopist planning specialized resectional procedures for lung cancer involving the bronchial tree. Whether CT is an appropriate screening test to determine if FOB or TTNA should be used in the diagnostic approach to a nodule is not clear. Future studies directly comparing the CT screening approach with an approach based on the bronchoscopist’s direct visual assessment are urgently needed before firm recommendations can be made.

**CT for Staging Mediastinal Nodes**

**CT for Detecting Mediastinal Nodes**

Not all mediastinal nodes can be detected by CT. Quint et al\(^{18}\) performed CT on five cadavers within 48 h of death and then meticulously dissected the mediastinum at autopsy. Most right-sided mediastinal nodes were detected by CT, but only 22 of 39 left-sided nodes found at autopsy were seen on CT.

![Figure 2. Depicted in this schematic are the hilar and mediastinal lymph node stations used in the American Thoracic Society staging system for lung cancer. Note that region 7 includes subcarinal lymph nodes.](image)

Because contrast agents were not infused during CT in this study, it may have been difficult to distinguish nodes from contiguous vascular structures. However, even with the use of intravenous contrast, experienced radiologists may have difficulty in identifying nodes within certain highly vascular mediastinal regions, eg, the aortopulmonary area. It is important to remember that detection of mediastinal nodes by CT depends not only on the technical characteristics of the scan itself and the ability of the radiologist to interpret the scan, but also on the adequacy of mediastinal evaluation at mediastinoscopy or thoracotomy. The more extensive the mediastinal dissection, the more likely the surgeon will find nodes not seen on CT.

Computed tomographic scans performed in subjects without lung cancer or granulomatous disease frequently reveal mediastinal lymph nodes. Nodes measured in these subjects in the transverse plane are usually smaller than 10 mm, with only a few larger than 10 mm. Normal lymph node size seems to vary by nodal region. Autopsy studies have shown that the largest nodes in normal subjects are found close to the hilum in regions 7, 4, and 10\(r\) (Fig 2). The maximal normal short-axis diameter for nodes in region 7 may be up to 12.3 mm. In areas of the world where granulomatous diseases are prevalent, mediastinal lymph node size may vary more widely.
nodes will be larger than this normal threshold. Many studies have confirmed that there is a substantial false-positive rate for CT staging of mediastinal nodes and, surprisingly, have shown that there is a similarly high false-negative rate. Just as enlarged nodes may be benign, a normal-sized node may contain metastatic tumor. Dales and colleagues performed a meta-analysis of the studies published between 1980 and 1988 that used CT for mediastinal staging and concluded that the overall sensitivity, specificity, and accuracy for these studies were about 80 percent. More recent studies have yielded similar results. Dales et al also analyzed which individual study variables might favor improved accuracy. Increasing the size threshold for an abnormal node seems to reduce the false-positive rate somewhat, but does not clearly improve overall accuracy. Improved CT technology was associated with an improved accuracy. Studies using a fourth-generation CT scanner, a scan time of less than 4 s, a scan thickness of less than 1 cm, and a scan spacing of less than 1 cm had overall sensitivity, specificity, and accuracy rates of 83 percent to 84 percent.

Other techniques have been used to improve the accuracy of CT mediastinal imaging. Several investigators have considered structural features of nodes as possible indicators of malignant spread. Benign nodes tended to have smooth, sharp, distinct borders, while malignant nodes were more likely to have a discontinue capsule or central necrosis. False-positive findings still occurred in these studies. Jolly et al used both a size threshold and the number of enlarged nodes as criteria for metastatic spread, but found little improvement in overall accuracy. Because lymph nodes normally vary in size among mediastinal regions, Ikezoe et al adjusted the cut-off size threshold for an abnormal node by nodal station and found a much improved specificity. König and colleagues used a sophisticated set of staging criteria incorporating both number of nodes and adjusted size threshold by region and reported a 100 percent specificity and a sensitivity of about 80 percent. Buy et al considered the size of nodes, the enlarged node’s location in relation to the primary tumor, and the size differential between the enlarged nodes and nodes in other regions in determining whether a node was abnormal. This approach was based on the pathologic observation that lung cancer tends to spread through mediastinal nodes along regional pathways, the pathway followed depending on the location of the primary tumor. Although surgical findings indicate that mediastinal metastases will frequently “skip” over the nodal regions draining the primary tumor, Buy et al noted a very low false-positive rate in their study.

The results of these studies suggest an encouraging

**CT for Distinguishing Benign From Malignant Nodes**

Because CT is a noninvasive imaging technique, it cannot provide direct histologic or cytologic evidence of malignant spread to mediastinal nodes. Nodal involvement by cancer can be inferred only from the size and structural features of CT visualized nodes. The most commonly used criteria for malignant nodal involvement is an enlarged node. The short-axis diameter of the node is usually the preferred indicator of pathologic enlargement for several reasons. The long-axis and short-axis diameter measurements will be influenced by the orientation of the node relative to the transverse plane of the CT image (Fig 3). Because mediastinal nodes tend to run in a cephalad-caudal direction, the long axis of these nodes would be less likely to be oriented in the CT transverse plane than the short axis. The coefficient of variation for short-axis diameter measurements is indeed less than for long-axis diameter measurements. The short-axis diameter also correlates better with node volume than the long-axis diameter and appears to be more accurate in distinguishing malignant from benign nodes than total cross-sectional nodal area.

The size threshold usually relied on for the upper-limit normal size of mediastinal node short-axis diameter is 10 mm. This limit is based on the CT studies in normal subjects and autopsy studies that showed that normal mediastinal nodes are infrequently larger than 10 mm in diameter. However, these studies also demonstrated that some benign

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**Figure 3.** Computed tomographic images are taken in the transverse plane. Lymph nodes that run in the cephalad-caudal direction will have their short axis oriented in the CT transverse plane. The long axis of these nodes will be more difficult to measure. Note that lymph nodes not running in a true cephalad-caudal direction will be sliced obliquely by the CT image. This is shown by comparing node 1 and node 2 in the diagram. Even though these nodes are the same size, because of node 2's oblique orientation, its short-axis and long-axis measurements on CT will be different from those of node 1.
trend. By improving CT technology, considering the number of enlarged mediastinal nodes, and adjusting the size threshold of an abnormal node by mediastinal region and location of the primary tumor, CT accuracy for mediastinal staging can be increased. This is achieved by improving specificity without sacrificing sensitivity. However, CT studies of mediastinal staging must be interpreted with caution. These studies tended to exclude patients with surgically unresectable disease. For instance, clinicians intuitively believe that patients with an abnormal mediastinum on CT have an unacceptably high rate of unresectable mediastinal disease. Consequently, they might not obtain a chest CT scan. Furthermore, patients with extensive mediastinal disease on CT might not be sent for an invasive diagnostic procedure to confirm cancer spread. In both these situations, a higher true-positive to false-positive ratio for CT scans would be expected. Excluding these patients will, therefore, artifactually alter CT operating characteristics. Because studies of consecutive patients with lung cancer that include both CT and histologic verification are generally not available, currently published CT operating characteristics for mediastinal staging should be accepted only as approximations. These CT studies have also not taken into account the effect lung inflammation associated with the carcinoma, eg, postobstructive pneumonia, might have on mediastinal node size. Recent work suggests that such inflammation may be an important stimulus for node enlargement.26,27

Clinicians rarely consider how well the standard CXR performs in distinguishing benign from malignant mediastinal nodes. Criteria for subcarinal node enlargement on CXR include increased subcarinal density, an abnormal azygoesophageal recess, and an obscured medial wall of the right mainstem bronchus and bronchus intermedius. When these criteria are used to evaluate how well the standard CXR performs in detecting subcarinal adenopathy in patients with enlarged nodes found on CT, CT appears to be more accurate. However, the specificity of CXR for subcarinal adenopathy is quite good.28

This observation points out important differences in the operating characteristics of CT and CXR (Table 4). Numerous authors have found that CT is better at detecting enlarged mediastinal nodes than CXR. Nodes must be substantially larger to be detected by CXR than CT. However, minimally enlarged nodes seen on CT but not CXR may not necessarily be malignant. Consequently, the false-positive rate for CT is higher than CXR. Conversely, the false-negative rate for CXR is lower than CT. Most studies confirm that the specificity of CXR for mediastinal disease is superior to CT, but the sensitivity is much worse. It should be noted that only CT studies incorporating size, location, and number adjustments in their criteria for abnormal mediastinal nodes have specificities similar to those reported by most CXR studies.

**Developing Strategies for Using CT in Mediastinal Node Staging**

The accepted approach to mediastinal node staging in lung cancer is based on the TNM classification system. The N in this scheme refers to the level of node involvement by tumor and is subclassified four ways. No evidence of nodal disease is designated N0. Tumor in hilar nodes only is classified N1 (lymph node station 11 in Fig 2). The N2 and N3 designations refer to different extents of mediastinal disease. Patients with N2 disease have tumor in ipsilateral mediastinal and subcarinal lymph nodes, while N3 disease encompasses disease in contralateral, scalene, and supraclavicular nodes. As N stage progresses, resectability becomes less likely and overall prognosis worsens.

Although the N system of mediastinal staging is

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Table 4—CXR vs CT for Staging the Mediastinum in Patients With Lung Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>CXR</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>Breyer*</td>
<td>56</td>
<td>33</td>
<td>100</td>
</tr>
<tr>
<td>Friedman*</td>
<td>45</td>
<td>67</td>
<td>100</td>
</tr>
<tr>
<td>Lewis*</td>
<td>418</td>
<td>40</td>
<td>99</td>
</tr>
<tr>
<td>Libshitz*</td>
<td>50</td>
<td>8</td>
<td>90</td>
</tr>
<tr>
<td>McKenna*</td>
<td>102</td>
<td>12</td>
<td>93</td>
</tr>
<tr>
<td>Moak*</td>
<td>41</td>
<td>54</td>
<td>86</td>
</tr>
<tr>
<td>Osborne*</td>
<td>42</td>
<td>5</td>
<td>100</td>
</tr>
<tr>
<td>Patterson*</td>
<td>84</td>
<td>81</td>
<td>43</td>
</tr>
<tr>
<td>Webb*</td>
<td>170</td>
<td>9</td>
<td>92</td>
</tr>
</tbody>
</table>

intuitively appealing because of its simplicity and clear relationship to prognosis, consensus on an overall approach or strategy for determining the N stage has eluded clinicians. Several principals are agreed on. Confirmation of node involvement should preferably be made by histologic or cytologic methods. An assessment of surgical resectability should be included with staging. Patients should be exposed to the least risk and expense possible during the staging process. Numerous mediastinal staging strategies have been offered as reasonable. Pearson et al.\(^{29}\) and Funatsu and colleagues\(^{30}\) favor mediastinoscopy routinely. In their experience, identification of abnormal nodes with this technique usually indicates extensive mediastinal disease and a poor chance for surgical cure. An important drawback to this approach is the expense and risk involved in mediastinoscopy, especially because many patients with lung cancer will have unresectable mediastinal disease.

Bronchoscopy with transbronchial needle aspiration (TBNA) may prove to be a less expensive and safer approach than mediastinoscopy for providing this same information,\(^{31}\) but whether a positive TBNA for malignancy has the same prognostic significance as a diagnostic mediastinoscopy is presently not clear. Other surgical groups strongly believe that mediastinoscopy is not an appropriate screening technique, because surgical resectability of mediastinal disease can only be assessed at thoracotomy.

An alternative view is that CT may be a useful noninvasive screening method for determining the need for mediastinoscopy. If no abnormal nodes were seen on CT, thoracotomy would be performed. If abnormal nodes were found, mediastinoscopy or TBNA directed by the CT results would be used as the intermediate step. An argument in support of this approach is the implicit belief that CT results can improve the results of mediastinoscopy and TBNA by guiding the operator toward enlarged nodes. Stronger support for this approach comes from recent studies. Cybulsky et al.\(^{32}\) raise the intriguing possibility that in patients with mediastinal metastases, the subgroup with enlarged nodes on CT have a worse prognosis for surgical cure. Daly and colleagues\(^{33}\) found that in patients with mediastinal disease discovered at thoracotomy, but with a benign mediastinum on prethoracotomy CT, the chances for curative resection were good.

At present, clinical studies directly comparing the various mediastinal staging strategies are not available. However, mathematical modeling techniques, \(te\), decision analysis, have been used to examine what role CT might play in staging the mediastinum in patients with lung cancer. Black et al.\(^{34}\) evaluated the role of CT in patients with clinical T1, N0, M0 tumors and found that CT did not substantially affect calculated life expectancy. Malenka and colleagues\(^{35}\) compared multiple strategies using various combinations of CT, mediastinoscopy, and bronchoscopy with TBNA for mediastinal staging. They also found that strategies using CT did not lead to an improved life expectancy. This finding, however, was probably expected because the analysis required that mediastinal nodal disease be verified histologically. In a subsequent study,\(^{36}\) this same group showed that basing therapeutic decisions solely on CT findings resulted in a worse life expectancy than found for strategies relying on invasive procedures for histologic verification of nodal disease.

Several important aspects of the work by Malenka et al.\(^{35,36}\) should be noted. The assumption that CT, by improving the accuracy of invasive diagnostic techniques, would improve outcome, \(te\), calculated life expectancy, was not supported by these decision analysis studies.\(^{35}\) Sensitivity analyses revealed that changing two variables would allow strategies relying on CT alone for mediastinal staging to achieve a calculated life expectancy approaching those for the histologically verified strategies. The key variable improving life expectancy was a CT specificity above 0.90. As discussed above, CT specificity in general is between 0.80 and 0.85. Studies using more sophisticated criteria than size alone to label nodes as abnormal have achieved specificities above 0.90. Unfortunately, to our knowledge, these studies have not been verified by other investigators. There are other noninvasive tests that probably have a specificity above 0.90 for mediastinal metastases. Most work with standard CXRs report a specificity above 0.90. A clinical evaluation (although not usually considered a noninvasive test) revealing hoarseness with a paralyzed left vocal cord, superior vena cava syndrome, dyspnea with a paralyzed diaphragm, or dysphagia indicates such a high probability of mediastinal metastases that many clinicians believe no further staging measures are necessary.

The other variable that greatly influenced life expectancy for mediastinal staging strategies relying on noninvasive methods was prevalence of mediastinal metastases.\(^{36}\) As Inouye and Sox have pointed out,\(^{37}\) the probability that an abnormal node identified by CT is malignant depends on both the operating characteristics of the CT scan and the prevalence of mediastinal disease in the study population. An abnormal node on CT in a patient with a high likelihood of mediastinal metastases will most probably be malignant, whereas an abnormal node in a patient with a low likelihood of such metastases will more probably be benign. The overall prevalence of mediastinal metastases in patients with newly recognized lung cancer can reasonably be estimated at about 40 percent. However, the prevalence rate
varies markedly in subgroups of patients with lung cancer.

A simple and reasonably reliable method for categorizing prevalence of mediastinal metastases is examining the CXR. The CXR findings that have the greatest bearing on the incidence of mediastinal node disease are interpretation of the mediastinum as either normal or abnormal, location of the primary tumor in either the central or peripheral lung field, and size of the primary tumor. The positive predictive value of an abnormal mediastinum on routine CXR for metastases to the mediastinum is so high, that a CT scan, whether its results are positive or negative, will do little to alter the very high probability that the patient does indeed have mediastinal nodal disease. Many authors have stated that performing a CT in a patient with an abnormal mediastinum on CXR adds little to the evaluation of the patient. In patients with a normal mediastinum on CXR the prevalence of mediastinal disease is lower for patients with peripheral primary tumors than central lesions and for small peripheral tumors than large ones. Most studies with few exceptions have shown that CT is rarely helpful in identifying metasatic mediastinal nodes in small peripheral lesions. In these cases, the CT false-positive rate is probably more of a hindrance in the evaluation of these patients than the true-positive rate is of importance. For patients with either a large peripheral tumor or a centrally located cancer and a normal mediastinum on CXR, the prevalence of mediastinal disease is probably intermediate.

These observations raise an intriguing point. Malenka et al36 identified two variables, specificity of the noninvasive diagnostic test and prevalence of mediastinal disease, which influence how well strictly noninvasive strategies for mediastinal staging perform. The standard CXR seems to perform better than CT in terms of specificity and probably similarly to CT in categorizing the prevalence of mediastinal disease. Given this information, perhaps the question that should be asked is whether CT adds appreciably to the CXR in the staging approach to the mediastinum. This is an especially pertinent question because Malenka et al35 also showed that mediastinal staging strategies using CT were consistently more expensive than other strategies achieving a similar life expectancy.

An important weakness in the work by Malenka and colleagues35,36 is that patients discovered to have mediastinal nodal disease were not offered the possibility of surgical resection in any of the decision trees considered. The surgical approach to lung cancer has evolved in recent years. Formerly, patients with mediastinal nodal involvement were considered to have unresectable conditions. Pioneering surgeons, however, have shown that reasonable 5-year survival rates can be achieved in selected patients with mediastinal nodal metastases following resection of the primary tumor and mediastinal lymphadenectomy. These results led to a revision of the lung cancer staging system. Ipsilateral and subcarinal nodal metastases are classified as N2 disease and the conditions of these patients are now at stage IIIa. They are considered potentially resectable. Contralateral mediastinal nodal metastases are classified as N3 disease. The conditions of these patients are at stage IIIb and are considered unresectable.

This revised staging system presents a new challenge to CT. Clinicians are no longer solely interested in whether mediastinal nodal metastases are present, they are also concerned with identifying those patients with mediastinal metastases who have surgically resectable conditions. There is little information available on how well CT distinguishes stage IIIa from stage IIIb disease. Watanabe et al39 operated on 153 patients with histologically verified mediastinal metastases and performed potentially curative resections in 84. Preoperative CT scans failed to identify abnormal nodes, ie, were false negative, in 37 percent of the patients undergoing curative resection and 23 percent of those patients who were not amenable to curative resection. The similar false-negative rates for the two groups indicate that CT has difficulty in detecting both resectable and unresectable mediastinal nodal metastases. When preoperative CT did detect abnormal mediastinal nodes in this study, the CT results could not be used to effectively distinguish resectable from unresectable disease.

Decision analysis studies have provided important insights into the limitations of using CT for mediastinal node staging. The value of using CT to improve the diagnostic accuracy of subsequent invasive diagnostic techniques has not been proved. The accuracy of CT for distinguishing resectable from nonresectable mediastinal disease has not been established. Furthermore, by identifying specificity and prevalence of mediastinal disease as the two key variables influencing the value of noninvasive mediastinal staging techniques, these decision analysis studies question the value of added information provided by CT beyond that available from the CXR. Because CT does not clearly perform better than standard CXR in either of these two variables, clinical decisions about evaluating the mediastinum might reasonably be based on interpretation of the CXR alone. For instance, patients with a high expected prevalence of mediastinal metastases, eg, those with an abnormal mediastinum on CXR or certain clinical manifestations, would not need CT for staging. If either mediastinoscopy or TBNA verify mediastinal metastases, curative resection is unlikely in these patients.
Conversely, for patients with a low expected prevalence of mediastinal metastases, eg, those with a small, peripheral tumor and a normal mediastinum on CXR, the critical issue is not whether mediastinal metastases are present, but whether they would be resectable. In these patients, because CT cannot reliably predict resectability of malignant nodes, the mediastinum should be carefully evaluated at thoracotomy for the presence and resectability of nodal metastases. Patients with a normal mediastinum on CXR and either a central tumor or a large peripheral tumor probably have an intermediate prevalence of mediastinal metastases. The performance characteristics of CT are not sufficiently good enough to either absolutely exclude or confirm mediastinal spread of disease in these cases. Again, evaluation of the mediastinum requires invasive testing.

In summary, the performance characteristics of CT for identifying malignant mediastinal nodes have been well described. Although there are encouraging trends indicating improvement in the accuracy of CT for mediastinal metastases, decision analysis studies suggest that CT at present should not be incorporated into strategies for mediastinal staging. The additional information provided by CT over that available in the standard CXR is not sufficient to justify its expense. Evaluating how CT should be incorporated into a comprehensive strategy for assessing the extent and resectability of mediastinal metastases in patients with lung cancer should be a high priority for future research.

CT for Detecting Invasion of Contiguous Structures

Numerous CT criteria have been proposed for identifying local invasion of contiguous structures by primary lung cancer. Unfortunately, consensus has not been reached over which, if any, of these criteria are useful for this purpose. Computed tomography visualizes pleural effusions well, but the presence of pleural fluid is a nonspecific finding. Pleural effusions may develop in various ways in lung cancer, including secondary toatelectasis, postobstructive pneumonia, and lymphatic obstruction. Only the presence of malignant cells in pleural fluid indicates unresectability. Computed tomographic findings consistent with parietal pleura and local chest wall invasion require that the primary tumor adjoin the chest wall and that there be some combination of either rib destruction, extension of a soft-tissue mass into the chest wall, increased density of extrapleural fat, an obtuse angle between the primary tumor and the chest wall, greater than 3-cm contact of tumor with pleura, an increased ratio of tumor pleural contact to tumor diameter, or thickened pleura. Evaluating the operating characteristics of these CT criteria for chest wall invasions is difficult, because most investigators have considered only patients with potentially resectable conditions, criteria have varied among studies, and study sizes have occasionally been small. Although some studies have reported a surprisingly high sensitivity and specificity for CT identifying chest wall invasion, in general, the CT results have been disappointing. Computed tomography may be somewhat more accurate than a standard CXR, but local pain may be as sensitive as CT for chest wall invasion. Ultrasound seems to perform far better than CT in identifying chest wall invasion by tumor. Recent surgical series indicate that primary tumors with parietal pleural invasion can be resected with expectations for reasonable survival rates. Computed tomographic criteria have not been developed for distinguishing resectable from unresectable parietal pleural spread as of yet. Little information is available on how well CT identifies invasion of either the diaphragm or pericardium.

Computed tomographic evaluation of direct mediastinal invasion by tumor is plagued by problems similar to those described above for identifying parietal pleural invasion. Studies have used incompletely stated criteria to exclude patients with nonresectable conditions, criteria have varied among studies, and study sizes have been occasionally small. Computed tomographic findings used to identify mediastinal invasion include the primary tumor contiguous with the mediastinum and any of such findings as interdigitation of the tumor with the mediastinal tissues, an obtuse angle at the junction of the tumor and the mediastinum, and indentations, notching, encasement, tapering, truncation, or scalloping of mediastinal vessels or bronchi. Even studies using multiple criteria, such as more than a 3-cm contact between tumor and mediastinum, a contact of the tumor with more than one quarter the circumference of the descending aorta, and absence of a mediastinal fat plane separating the tumor from mediastinal structures, have not proved to be highly accurate in identifying mediastinal invasion. Again, however, the clinical question is whether CT can distinguish resectable from unresectable mediastinal invasion. It is clear that some patients are not considered surgical candidates because of CT findings. It has also been suggested that CT has led to a decrease in the number of unsuccessful thoracotomies for cure in lung cancer. Unfortunately, criteria for determining unresectable from resectable conditions in patients have not been defined. Patients with an abnormal mediastinum on CT may have a resectable condition at thoracotomy.

Computed tomography may better delineate tumor spread in the superior sulcus than standard CXR, but CT does not perform as well as magnetic
resonance imaging (MRI) in this regard. The multiplanar capability of MRI allows for direct imaging of the superior sulcus tumor in the coronal and sagittal planes, allowing better assessment of the cephalad tumor extent. Magnetic resonance imaging also allows better delineation of the brachial plexus and the spinal cord and more clearly demonstrates the relationship of the superior sulcus tumor to nearby vessels.\textsuperscript{43–45}

In summary, CT criteria are not well established for distinguishing unresectable from resectable invasion of the parietal pleura, diaphragm, pericardium, and mediastinum. Resectability should be based on the surgeon’s assessment at thoracotomy. For tumors of the superior sulcus, MRI is better suited to evaluate preoperative extent of disease than CT.

CONCLUSION

Computed tomography is a remarkable technique for visualizing structures within the thorax. Intensive interest over the past decade has been focused on using CT to evaluate suspected and known lung cancer. Unfortunately, despite efforts by many investigators, it is still not entirely clear how CT should be used to detect and manage bronchogenic carcinoma. Further technological refinements are not sufficient. Careful experimentation must be directed toward establishing strategies for using CT to distinguish benign from malignant chest lesions and to stage and manage the intrathoracic components of lung cancer. These strategies should include estimates of cost-effectiveness as well as clinical reliability.

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NOTE: The manuscript includes only an abridged reference list. A complete bibliography is available on request from the author.

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