Imaging Bronchogenic Carcinoma*

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Imaging plays an integral role in diagnosing, staging, and following patients with lung cancer. Most lung tumors are detected on chest radiographs, but unfortunately, the majority of patients have advanced stage disease at presentation. There is a wide spectrum of radiologic manifestations of lung cancer, and recognition of these findings is essential for patient management. As we continue to understand more about tumor biology, new imaging techniques should emerge and have the potential to significantly improve our diagnostic capabilities. *(CHEST 2000; 117:90S–95S)*

**Key words:** CT; diagnostic imaging; lung cancer; positron emission tomography

**Abbreviations:** BAC = bronchioloalveolar cell carcinoma; FDG = F-18-fluorodeoxyglucose; NSCLC = non-small cell lung cancer; PET = positron emission tomography; SCLC = small cell lung carcinoma

**Bronchogenic carcinoma,** an uncommon disease at the turn of the 20th century (only several hundred cases reported before 1900), has become a major health problem heading into the new millennium. Approximately 172,000 new cases will occur this year in the United States alone.1–3 The diagnosis of lung cancer has relied on detection of cells in sputum or biopsy specimens and, perhaps more importantly, on specific findings observed on chest radiographs. The purpose of this review is to describe the radiographic features of bronchogenic carcinoma for diagnosis and staging.

**Diagnostic Evaluation**

Lung cancer is often considered in the differential diagnosis for a spectrum of thoracic radiographic abnormalities. When an abnormality is detected, an important next step is comparison with old radiographs. Most consider a 2-year interval without change as good evidence for benignancy.4,5 Occasionally, the lesion has a benign pattern of calcification (central, concentric, or stippled appearance), or clinical information suggests a specific diagnosis.

If no old radiographs are available, or if the abnormality is new, CT may further characterize the lesion. While CT is extremely specific for certain benign lesions, most abnormalities remain indeterminate and lung cancer cannot be excluded. Patients may then proceed to an invasive procedure for diagnosis.

Recently, a noninvasive test, positron emission tomog-

raphy (PET) imaging, has been used to evaluate pulmonary lesions. PET using F-18-fluorodeoxyglucose (FDG), a d-glucose analog, is very accurate in differentiating benign from malignant focal pulmonary lesions as small as 1 cm (sensitivity of 83 to 100%, and specificity of 80 to 100%6–8 and may prove to be very cost-effective.9 False-positive studies (eg, increased FDG in benign lesions including aspergillomas, abscesses, tuberculosis, and histoplasmosis6,8,10–13) have been reported; however, when no significant FDG activity is observed, the lesions are invariably benign. These abnormalities can be followed; invasive procedures are not necessary. Hypermetabolic lesions are considered malignant until proven otherwise, usually by tissue diagnosis.

**Non-Small Cell Lung Carcinoma**

Non-small cell lung carcinoma (NSCLC) accounts for approximately 80% of all bronchogenic carcinomas, and is typically classified into specific cell types. The most common types are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma, although a variety of other unusual cell types have been classified according to the World Health Organization.14

**Adenocarcinoma:** Adenocarcinoma accounts for 25 to 30% of NSCLC and is the most common type.15 It is typically classified as acinar, papillary, solid, and bronchioloalveolar varieties. Adenocarcinoma typically presents as a small (often < 4 cm), peripheral, round or oval, smoothly marginated, solitary pulmonary nodule. Occasionally, a more central location or spiculation and irregular margins are noted. Some lesions distort surrounding vessels (corona radiata) or cause retraction of the adjacent pleura (“pleuroparenchymal tail”), but these features also may be seen with benign abnormalities.16–18

Calcification is rarely seen in lung cancer on chest radiographs; however, eccentric or amorphous calcification has been reported in up to 6% of cases at CT. Calcification at times represents engulfment of a preexisting granuloma.19–21

With peripheral adenocarcinoma, lymphadenopathy is seen in 18% and 2% of hilar and mediastinal lymph nodes, respectively.20,22 Central lesions, however, have hilar nodal metastases in 40% of cases, and mediastinal lymph node metastases in 27% of cases.17,20

Bronchioloalveolar cell carcinoma (BAC) is a peculiar subtype of adenocarcinoma that may present with solitary or multiple lesions.23 The chest radiographs of patients with BAC most commonly demonstrate a well-circumscribed solitary nodule (60%) that may remain unchanged in size over several years.17,24–25 BACs, like the majority of adenocarcinomas, are usually peripherally located.26,27 Pseudocavitation, the presence of small focal low-attenuation regions within or surrounding the periphery of the nodule and air bronchograms, is more commonly associated with these tumors than other cell types.

Multifocal BAC may present as follows: (1) multiple well-defined nodular opacities of varying size, including one or both lungs (15%);26,27 (2) focal, poorly defined opacities or multiple scattered opacities17 that may

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coalesce into lobar and rarely complete lung opacification,\textsuperscript{16} resembling pneumonia (10%); or (3) reticulonodular opacities resembling interstitial lung disease. Other radiographic features include hilar and mediastinal metastases (18%), pleural effusions (1 to 10%), atelectasis (3%), and rarely pneumothorax.\textsuperscript{16,26}

\textbf{Squamous Cell Carcinoma:} Squamous cell carcinoma has decreased in frequency and now comprises 25\% of lung cancers.\textsuperscript{15} These are usually slow growing, with late metastasis predominately to the liver, adrenal glands, kidneys, and bones.\textsuperscript{16,31} Tumors usually range in size from 1 to 10 cm. They are typically found in the central bronchi, although one third occur beyond the segmental bronchi.\textsuperscript{16,17,22} Endobronchial neoplasm may result in postobstructive pneumonia and/or atelectasis in up to 50\% of cases,\textsuperscript{16,22,32} and the underlying mass may be observed.\textsuperscript{16,32} Mucoid impaction, bronchiectasis, and hyperinflation are additional findings of a central obstructing neoplasm.\textsuperscript{16,17,33,34} Extension into the chest wall or mediastinum with bone destruction, superior vena cava syndromie, and phrenic or recurrent laryngeal nerve paralysis have been reported.\textsuperscript{16,23,30}

Squamous cell carcinoma cavitates in 10 to 20\% of cases,\textsuperscript{16,22} particularly in large peripheral lesions (30\%).\textsuperscript{16,17,22,35} Cavity walls are usually thick and irregular, ranging in size from 0.5 to 3 cm. Rarely, extensive necrosis may result in a thin-walled cavity.\textsuperscript{16}

Squamous cell carcinoma is the most common type to prove Pancoast or superior sulcus tumors.\textsuperscript{16} Asymmetry of $> 8$ mm in apical pleural thickening may be an important finding, especially when associated with chest wall pain, brachial or laryngeal nerve paralysis, or bone destruction.\textsuperscript{16}

\textbf{Large Cell Carcinoma:} Approximately 10 to 20\% of all lung cancers are large cell carcinomas.\textsuperscript{16,19,30} The majority present as a large (average size $> 7$ cm), peripheral mass,\textsuperscript{16,17,19,22,31,36,37} with poorly defined margins. Cavitation and calcification are uncommon (6\%). Hilar and mediastinal adenopathy are seen in 30\% and 10\% of cases, respectively.\textsuperscript{16,17,19,22,32} Rapid growth with early lymphatic and hematogenous metastases occurs frequently.\textsuperscript{37}

\textbf{Small Cell Lung Carcinoma}

Twenty to 25\% of all lung cancers are small cell lung carcinoma (SCLC).\textsuperscript{19,30,38} They probably arise from neuroendocrine cells and contain neurosecretory granules and may produce peptide hormones.\textsuperscript{23,30}

The tumors are usually located centrally (75 to 90\% of cases),\textsuperscript{19,39} and mediastinal extension is common and often extensive with encasement of mediastinal structures and tracheobronchial compression.\textsuperscript{40,44} The less-commonly described peripheral SCLC is often associated with hilar adenopathy.\textsuperscript{16,19,22,30} and atelectasis secondary to main stem bronchus compression.\textsuperscript{17,19} Pleural effusions are reported in 5 to 50\% of cases.\textsuperscript{16,40–42}

The primary lesion may be small or not even visible on radiograph studies, but early extrathoracic metastases are common and even present prior to the development of pulmonary symptoms.\textsuperscript{23,30} Liver, bone marrow, adrenal glands, and brain are frequent sites of metastatic disease.\textsuperscript{19,39}

\section*{Staging Evaluation}

\textbf{NSCLC}

When bronchogenic carcinoma has been diagnosed, accurate staging becomes essential for therapeutic decision making and prognosis estimation. The new International System for Staging Lung Cancer using a TNM system has provided a standardized method to describe anatomic extent of disease.\textsuperscript{43–48} Radiologic studies used in conjunction with the International System for Staging Lung Cancer include chest radiographs, CT, and occasionally MRI. The appropriate role of imaging in management still requires definition, but the major indication is to accurately differentiate stage I to IIIA (potentially resectable) from stage IIIB to IV (nonresectable) cancer.\textsuperscript{49–51}

\textbf{Local Disease (Size and Extent; T Status):} Radiologic assessment of the size of primary lesions is usually done using plain chest radiographs and, less commonly, CT or MRI. Measurements may be inaccurate secondary to ill-defined margins, change in rotation or degree of inspiration, window-setting differences on CT, or other factors, but are generally valuable for purposes of tumor staging.

The extent of primary lesion can be suggested by plain radiographs, CT, and MRI, but may not necessarily be accurate in confirming chest wall or local mediastinal invasion unless a chest wall mass, rib destruction, or gross encasement of mediastinal structures is present.\textsuperscript{52–54} The overall accuracy of CT in confirming invasion has been reported to be 39 to 86\%.\textsuperscript{12,54–56} An advantage of MRI in evaluating chest wall invasion is its superior soft-tissue contrast resolution and multiplanar capability.\textsuperscript{59,60} MRI has sensitivity (63 to 90\%) and specificity (84 to 86\%) similar to CT,\textsuperscript{12,61,62} but is better than CT when findings are equivocal.\textsuperscript{56,63} MRI is particularly useful in evaluation of superior sulcus tumors, as CT is limited by its axial format and streak artifacts from the shoulders. In this setting, MRI can accurately assess the extent of local invasion, including brachial plexus and subclavian vessel involvement.\textsuperscript{56,59,61,64–66} Vertebral body marrow invasion, a finding that would preclude resection, is also optimally assessed by MRI.\textsuperscript{65}

CT and MRI have similar accuracies in diagnosing mediastinal involvement (56 to 59\% and 50 to 93\%, respectively), although MRI has been shown by the Radiologic Diagnostic Oncology Group trials to be slightly better.\textsuperscript{56,61,67–69} T1-weighted images optimally demonstrate tumor invasion of mediastinal fat, and mediastinal involvement adjacent to a hilar mass is easier to determine at MRI due to contrast between the neoplasm and flow void in vessels.\textsuperscript{65,70}

\textbf{Nodal Disease (N Status):} CT and occasionally MRI are used to evaluate the hilar and mediastinal lymph nodes. Size, unfortunately a nonspecific criterion, is the only criterion used in attempting to distinguish normal
from abnormal lymph nodes (short axis > 1 cm is considered abnormal).\textsuperscript{71} Lymph node morphology and MRI signal characteristics are not useful in predicting lymph node metastases.\textsuperscript{12} Although CT and MRI are very accurate in demonstrating enlarged lymph nodes, the cause of enlargement may be reactive hyperplasia, not metastasis, particularly if there is a postobstructive pneumonia.\textsuperscript{64,72} The accuracy of CT and MRI for detecting metastatic hilar (N1) disease is only 62 to 68\% and 68 to 74\%, respectively.\textsuperscript{67,73} This low accuracy of radiographic staging of N1 metastatic disease, in most cases, does not prevent surgical resection unless the patient is a poor surgical candidate.\textsuperscript{12,72}

The limitation of chest radiographs and CT/MRI, their dependence on morphologic and anatomic findings, may occasionally be overcome by FDG-PET imaging (Fig 1).\textsuperscript{6,7} PET has recently been demonstrated to be more accurate than CT in diagnosing the presence of intrathoracic metastatic nodal disease (81\% and 52\%, respectively).\textsuperscript{6,74} In another study, large nodes at CT were shown to be nonmetastatic in 100\% of patients when the nodes were not FDG avid. In addition, the positive predictive value for metastases was 100\% for CT-detected small nodes that had intense FDG uptake.\textsuperscript{75}

**Metastatic Disease (M Status):** Common sites of metastases are lymph nodes as described above; brain and CNS, bone, and adrenal gland metastases and metastases to the contralateral lung are considered M1 disease.\textsuperscript{56} Initiating a radiologic investigation for metastatic disease is often based on the clinical history, physical examination, and blood indexes (CBC count, alkaline phosphatase, liver

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**FIGURE 1.** Top, left: Posteroanterior chest radiograph of 66-year-old man who presented with a cough, demonstrating an irregular 3.5-cm mass in the right base (arrow). Top, right: Coronal whole body PET image demonstrates significant FDG uptake in the right lower lobe mass (arrow). In addition, there is a smaller area of increased uptake in the right humerus and a second small area of abnormal uptake in the right apex. The patient had no signs of bony or metastatic disease, although plain radiographs of the right arm initiated from the PET study demonstrate a small lytic lesion in the right humerus consistent with metastasis. Note is made of expected increased FDG activity in the left wrist at the injection site, and in the kidneys and bladder from FDG excretion. Bottom, left: Axial CT image through the dome of the liver demonstrates a small low attenuation area in the liver (arrow) and slight soft tissue fullness in the right adrenal gland (arrow head). Bottom, right: Axial PET image at the same level demonstrates significant FDG uptake in both the liver lesion (arrow) and adrenal mass (arrow head), consistent with metastatic disease.
function tests). \textsuperscript{49,76} Routine radiologic evaluation for occult metastases in the absence of clinical or laboratory findings is not clearly indicated. \textsuperscript{49,50,56,76}

Isolated CNS metastases are rare in patients with NSCLC and are generally associated with an abnormal neurologic examination. \textsuperscript{36,77} Asymptomatic brain metastases occur in 2.7 to 9.6% of patients usually with large cell carcinomas and adenocarcinoma. The use of routine CT or MRI of the CNS in asymptomatic patients with NSCLC is controversial. \textsuperscript{77–80}

Patients with bone metastases are usually symptomatic (pain) or have suggestive laboratory abnormalities (eg, elevated alkaline phosphatase). \textsuperscript{80} Bone radiographs, radionuclide bone scanning with 99 technetium-methylene diphosphonate or MRI are useful modalities for further evaluation. \textsuperscript{49} Occult skeletal metastases are rarely (up to 4%) detected by radionuclide 99 technetium-methylene diphosphonate studies, but there is a high false-positive rate (approximately 40%). \textsuperscript{76,77,70,80} Thus, routine radionuclide skeletal imaging should not be performed in NSCLC.

Adrenal metastases do not produce reliable clinical and laboratory findings; thus, upper abdominal imaging is routinely performed, especially as part of thoracic CT staging. Incidental nonfunctioning cortical adenomas occur in 3 to 5% of the population, and approximately 10% of patients with NSCLC will have an adrenal mass at CT. \textsuperscript{50,81,82} In the absence of other known extrathoracic metastases, an adrenal mass is more likely benign. Attenuation values \(\leq 10\) are virtually pathognomonic benign adrenal enlargement. \textsuperscript{56,81} CT and MRI are similar in detecting hepatic metastases, although isolated liver metastases are extremely uncommon and routine liver imaging is not usually suggested. \textsuperscript{50,83,84}

\textbf{SCLC}

Radiologic staging of SCLC may help in determining prognosis and in treatment planning. \textsuperscript{85} A two-stage classification proposed by the Veteran’s Administration Lung Cancer Study Group separating patients into limited or extensive disease groups has proven useful. \textsuperscript{86} Limited disease is defined as tumor within a single radiotherapy port (tumor confined to the thorax). Extensive disease includes distant metastases and noncontiguous metastases to the contralateral lung. \textsuperscript{48,86} Long-term survival occurs primarily with limited disease and is rare with extensive disease. \textsuperscript{86}

Extensive disease is present at presentation in 60 to 80% of patients with SCLC. \textsuperscript{56,85,87,88} Metastases commonly occur in the liver (22 to 25%), bone (30 to 38%), bone marrow (17 to 25%), brain (8 to 15%), and retroperitoneal lymph nodes (11%). \textsuperscript{85–89} Conventional clinical and radiographic evaluation of extrathoracic metastatic disease usually includes bone marrow aspiration, radionuclide bone scan, and CT or MRI of the brain and abdomen. \textsuperscript{56,85,90} MRI alone has recently been used as an accurate staging modality for liver, adrenals, brain, and axial skeleton. Liver function tests can be normal with hepatic metastases, and 25% of patients presenting with hepatic metastatic disease will not have involvement of other organs. \textsuperscript{86} Abdominal CT or ultrasound should be done routinely in the staging evaluation of SCLC. \textsuperscript{86} MRI may be more sensitive than contrast-enhanced CT in detecting hepatic metastases, and similar to CT in evaluation of adrenal metastases. \textsuperscript{85}

Isolated bone and bone marrow metastases are uncommon and are usually associated with involvement of other organs. \textsuperscript{86,90} These patients often have no focal bone pain, and alkaline phosphatase and peripheral blood findings are usually normal. \textsuperscript{86,90} Consequently, if there are extrathoracic metastases, further evaluation should include a radionuclide bone scan and bone marrow aspiration. MRI may be more sensitive than bone scintigraphy in detecting small and rapidly growing metastases with marrow infiltration. \textsuperscript{55,91}

CNS metastases are common at presentation and as a site of future disease. \textsuperscript{86} Routine CT or MRI evaluation of the CNS is recommended, as approximately 5% of patients with cerebral metastases are asymptomatic. \textsuperscript{92} In NSCLC, 2.7 to 9.6% are symptomatic and use of imaging is controversial. Detection and treatment with aggressive chemotherapy and radiotherapy can decrease morbidity and improve prognosis if the brain is the only site of extrathoracic disease. \textsuperscript{86}

\textbf{Conclusion}

Current imaging for bronchogenic carcinoma makes use of plain chest radiographs, CT, MRI, and nuclear medicine. Most studies are designed to detect anatomic abnormalities, leading to some problems in sensitivity and especially specificity. In the future, imaging may be directed more at tumor biology (molecular and genetic targets), and perhaps then will have a greater impact on this devastating disease.

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