

**American College of Radiology
ACR Appropriateness Criteria®
Noninvasive Clinical Staging of Primary Lung Cancer**

Variant: 1 Noninvasive initial clinical staging of non-small-cell lung carcinoma.

| Procedure | Appropriateness Category | Relative Radiation Level |
|--|--------------------------|--------------------------|
| MRI head without and with IV contrast | Usually Appropriate | 0 |
| CT chest with IV contrast | Usually Appropriate | ☼☼☼ |
| CT chest without IV contrast | Usually Appropriate | ☼☼☼ |
| FDG-PET/CT skull base to mid-thigh | Usually Appropriate | ☼☼☼☼ |
| MRI abdomen without and with IV contrast | May Be Appropriate | 0 |
| MRI abdomen without IV contrast | May Be Appropriate | 0 |
| MRI chest without and with IV contrast | May Be Appropriate | 0 |
| MRI head without IV contrast | May Be Appropriate | 0 |
| Bone scan whole body | May Be Appropriate | ☼☼☼ |
| CT abdomen and pelvis with IV contrast | May Be Appropriate | ☼☼☼ |
| CT abdomen and pelvis without IV contrast | May Be Appropriate | ☼☼☼ |
| CT head with IV contrast | May Be Appropriate | ☼☼☼ |
| CT head without and with IV contrast | May Be Appropriate | ☼☼☼ |
| CT abdomen and pelvis without and with IV contrast | May Be Appropriate | ☼☼☼☼ |
| Radiography chest | Usually Not Appropriate | ☼ |
| MRI chest without IV contrast | Usually Not Appropriate | 0 |
| CT chest without and with IV contrast | Usually Not Appropriate | ☼☼☼ |
| CT head without IV contrast | Usually Not Appropriate | ☼☼☼ |

Variant: 2 Noninvasive initial clinical staging of small-cell lung carcinoma.

| Procedure | Appropriateness Category | Relative Radiation Level |
|--|--------------------------|--------------------------|
| MRI head without and with IV contrast | Usually Appropriate | 0 |
| CT abdomen and pelvis with IV contrast | Usually Appropriate | ☼☼☼ |
| CT chest with IV contrast | Usually Appropriate | ☼☼☼ |
| FDG-PET/CT skull base to mid-thigh | Usually Appropriate | ☼☼☼☼ |
| MRI abdomen without and with IV contrast | May Be Appropriate | 0 |
| MRI abdomen without IV contrast | May Be Appropriate | 0 |
| MRI chest without and with IV contrast | May Be Appropriate | 0 |
| MRI head without IV contrast | May Be Appropriate | 0 |
| Bone scan whole body | May Be Appropriate | ☼☼☼ |
| CT abdomen and pelvis without IV contrast | May Be Appropriate | ☼☼☼ |
| CT chest without IV contrast | May Be Appropriate | ☼☼☼ |
| CT head with IV contrast | May Be Appropriate | ☼☼☼ |
| CT head without and with IV contrast | May Be Appropriate | ☼☼☼ |
| CT abdomen and pelvis without and with IV contrast | May Be Appropriate | ☼☼☼☼ |
| Radiography chest | Usually Not Appropriate | ☼ |
| MRI chest without IV contrast | Usually Not Appropriate | 0 |

| | | |
|---------------------------------------|-------------------------|-----|
| CT chest without and with IV contrast | Usually Not Appropriate | ☹☹☹ |
| CT head without IV contrast | Usually Not Appropriate | ☹☹☹ |

Panel Members

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Summary of Literature Review

Introduction/Background

Lung cancer is the leading cause of cancer-related deaths in both men and women. While the incidence of the disease for men in the United States has been steadily decreasing since the 1970s, the incidence for women in the United States increased after 1975 before leveling in the 2000s [1]. The major risk factor for lung cancer is personal tobacco smoking, particularly for small-cell lung cancer (SCLC) and squamous-cell lung cancers, but other significant risk factors include exposure to second-hand smoke, environmental radon, occupational exposures, and air pollution. Education and socioeconomic status affect both incidence and outcomes, with a disproportionate amount of the disease burden seen in the poor and poorly educated. The economic cost of caring for lung cancer patients in the United States is over \$12 billion per year. Mortality cost from lost productivity also numbers in the billions of dollars [2].

Non-small-cell lung cancer (NSCLC), including adenocarcinoma, squamous-cell carcinoma, and large-cell carcinoma, comprises about 85% of lung cancers. SCLC accounts for approximately 13% to 15% of cases. Prognosis is directly related to stage at presentation, with 5-year survival ranging as high as 77% for small stage IA cancers to 1% to 2% for stage IV lung cancer [3]. The majority of lung cancer patients present with advanced disease. Selection of appropriate treatment options including curative surgery, radiation therapy, chemotherapy, targeted therapy, or multimodality therapy is increasingly influenced by pathologic evaluation with immunohistochemical staining but remains dependent on accurate staging.

Discussion of Procedures by Variant

Variant 1: Noninvasive initial clinical staging of non-small-cell lung carcinoma.

NSCLC is staged using the eighth edition of the tumor-node-metastasis (TNM) criteria of the American Joint Committee on Cancer, developed under the auspices of the International Association for the Study of Lung Cancer and informed by database analysis of nearly 95,000 patients primarily from Europe and Asia [4]. Clinical noninvasive staging by radiologic imaging is the first step in determining the appropriate management for patients with lung cancer.

T Descriptor

The T descriptor is based on size and location of the primary tumor, the presence or absence of atelectasis or postobstructive pneumonitis, and the degree of invasion into adjacent structures exhibited by the primary tumor [5,6].

- T0 describes no evidence of a primary lung tumor [5].
- Tis describes carcinoma in situ, either squamous cell or adenocarcinoma [5].
- T1 comprises tumors ≤ 3 cm in greatest dimension, subdivided into four categories: (1) T1a(mi) is minimally invasive lepidic-predominant adenocarcinomas ≤ 3 cm with ≤ 0.5 cm invasion in any single focus; (2) T1a are tumors ≤ 1 cm; (3) T1b tumors are > 1 cm to ≤ 2 cm; and (4) T1c are tumors > 2 cm to ≤ 3 cm [5].
- T2 tumors are > 3 to ≤ 5 cm, with T2a categorized as tumors > 3 cm to ≤ 4 cm, while T2b tumors are > 4 cm to ≤ 5 cm. T2 tumors may be with or without visceral pleural invasion. Other features that pertain to T2 include atelectasis or obstructive pneumonitis extending to the hilum and endobronchial tumors involving a main bronchus any distance from the carina but without carinal involvement [5].
- T3 tumors are > 5 cm to ≤ 7 cm in size. In addition, ipsilateral satellite nodule in the same lobe as the primary tumor is considered T3 disease. Invasion of the chest wall, phrenic nerve, parietal pleura or pericardium are also T3 [5].
- T4 tumors are those > 7 cm or which invade the carina, diaphragm, vertebral bod(ies), or mediastinal structures including heart, trachea, esophagus, and recurrent laryngeal nerve. Ipsilateral satellite nodules in a different lobe from the primary tumor signify T4 lesions [5].

N Descriptor

The eighth edition makes no changes from the previous edition with regard to metastatic nodal disease. The N stage is based on location of metastatic nodes. Increasing number of involved nodal stations negatively affects prognosis [5]. A lymph node size threshold of > 10 mm in axial short axis diameter is considered abnormal. The prevalence of metastatic lung cancer in thoracic lymph nodes is 30% for nodes that are 10 to 15 mm in short axis diameter and 67% for nodes > 15 mm [7]. Axillary lymph node metastasis occurs in 0.75% of lung cancers [8]. It is not included in the N descriptor but is considered metastatic M1 disease.

- Nx indicates that lymph nodes cannot be assessed [5].
- N0 is consistent with lack of regional node involvement [5].
- N1 includes ipsilateral peribronchial, hilar or intrapulmonary lymph node(s) [5].
- N2 describes ipsilateral mediastinal or subcarinal lymph node(s) [5].
- N3 includes contralateral mediastinal or hilar lymph node(s) and any supraclavicular or scalene node on either side [5].

M Descriptor

The presence of metastatic lung cancer lesions constitutes stage IV disease. Many patients with NSCLC present with metastatic disease [9], and the treatment of stage IV cancers depends on the location and number of lesions.

- M0 disease is consistent with no distant metastases [5].

The M1 classification is subdivided into three categories:

- M1a includes satellite nodule(s) in the contralateral lung and cytology proven malignant pleural or pericardial effusion [5].
- M1b indicates a single extrathoracic metastasis. This category also includes metastasis in a

single nonregional lymph node, considered nodes not in the N descriptor, such as enlarged axillary, internal mammary, and/or abdominal lymph node [5,6].

- M1c indicates multiple extrathoracic metastases in one or more organs [5].

Stage Groups for NSCLC

Stage groupings have been revised according to statistically significant differences in survival among tumors in the database. The eighth edition includes new differentiation among stage IA tumors based on size of the tumor and a new stage IIIC category for T3 and T4 tumors with N3M0 disease [6].

The eighth edition also includes staging information for patients with multifocal ground-glass nodules representing multiple synchronous adenocarcinomas with lepidic-predominance, including adenocarcinoma in situ, minimally invasive adenocarcinoma, and lepidic-predominant adenocarcinoma. The T descriptor is based on the size of the largest lesion. The total number of lesions should be indicated with the letter 'm' for multiplicity in parentheses (#/m). The N and M descriptors are combined for all tumors, so only a single N and M will be reported [5,10].

Classification of mucinous adenocarcinomas is also addressed. The T descriptor is based on size if confined to a single lobe. The tumor is designated as T3 if size cannot be determined but remains in a single lobe. Involvement of multiple ipsilateral lobes is T4 disease. Bilateral lesions are considered M1a [5,10].

Variant 1: Noninvasive initial clinical staging of non-small-cell lung carcinoma.

A. CT Chest

For patients with known or suspected NSCLC, a chest CT with intravenous (IV) contrast is recommended. A chest CT without IV contrast may also be obtained.

Chest CT is the modality of choice for initial evaluation of the T descriptor, specifically the size and location of the primary tumor. Diagnosis of chest wall or mediastinal invasion on CT can be equivocal in cases of minimal invasion. Radiologic imaging cannot consistently detect visceral pleural invasion.

Chest CT with IV contrast can aid in the identification of mediastinal or chest wall invasion by tumor, evaluation of hilar lymph nodes, distinction of central obstructing tumor from surrounding atelectasis, and assessment for liver metastases [11,12]. Chest CT without IV contrast is often better able to characterize adrenal nodules than chest CT with contrast, but the benefit of a noncontrast chest CT for this purpose may be obviated by performance of PET or PET/CT.

Accurate N staging of the mediastinum is important in distinguishing resectable from unresectable disease. CT staging of nodal disease in the mediastinum is inadequate because of its low sensitivity and specificity of anatomic size criteria [11]. A meta-analysis of over 7,000 patients found that the prevalence of mediastinal lymph node metastasis was 30%. However, the median sensitivity of contrast-enhanced CT was 55%, and median specificity was 81% for mediastinal nodal disease using the >10-mm short axis diameter criteria [11]. Findings on chest CT of enlarged mediastinal nodes aids in guiding biopsy, as invasive staging of the mediastinum is recommended over imaging alone [11].

The distribution of mediastinal lymph node metastases is influenced by the location of the primary tumor. Right upper lobe tumors drain to the right paratracheal nodes (2R and 4R), while right middle and lower lobe tumors most frequently drain to the lower right paratracheal and subcarinal nodes (4R and 7R). Nodal metastases for the left upper lobe are most often seen in the aortopulmonary window and prevascular nodes (5L and 6L). Left lower lobe tumors drain to the prevascular and subcarinal nodes (6L and 7L) [13]. Tumors in the lower lobe superior segments frequently have upper mediastinal lymph node involvement (64%) compared with basal segment tumors [14].

Chest CT is adequate for the identification of contralateral lung nodules constituting M1a disease. It also identifies pleural or pericardial effusions that may need cytological confirmation if pleural or pericardial nodules are not visible. Extrathoracic M1b metastases of the adrenal glands and bone structures may be seen on a chest CT. However, adrenal nodules may not be definitively characterized by CT if IV contrast is used or if intracytoplasmic lipid content is low, which occurs in approximately one-third of adrenal adenomas. Techniques for further evaluation include PET using the tracer fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) with CT, CT adrenal washout protocol, and MR chemical shift of in- and out-of-phase imaging [15]. Liver metastases may be seen if they occur within the included segments on chest CT and are better identified on contrast-enhanced studies, particularly if lesions are small.

VARIANT 1: Noninvasive initial clinical staging of non-small-cell lung carcinoma. **B. FDG-PET/CT Skull Base to Mid-Thigh**

FDG-PET/CT is recommended to evaluate for extrathoracic metastases in patients with NSCLC. It is not required for patients with stage 0 adenocarcinoma in situ with an otherwise normal chest CT examination.

FDG-PET is reported to change management in 14% to 26% of NSCLC patients [16-18]. FDG-PET imaging is superior to CT in detection of nodal and distant metastases [19]. FDG-PET may upstage NSCLC by identifying metastases that were occult on CT imaging or downstage the malignancy by demonstrating lack of glucose metabolism in a suspected lesion [20]. Integrated FDG-PET/CT is more accurate for staging of the N and M descriptors than independent FDG-PET or diagnostic CT [21]. FDG-PET or PET/CT is reported to reduce futile thoracotomies by 20% and 17%, respectively [19,22].

Lymph nodes are considered abnormal on FDG-PET or PET/CT if they have increased FDG uptake, regardless of size. There is no validated standardized uptake value threshold for positive activity in thoracic lymph nodes [23]. Meta-analysis has reported specificity of FDG-PET of 92% for mediastinal node metastases, with sensitivity of 83% [24]. False-positive FDG activity in lymph nodes can occur as the result of infectious or inflammatory causes [25]. FDG-PET/CT for staging should ideally be performed within 60 days of any planned resection and within 30 days before radiation therapy, as sensitivity and accuracy for nodal staging is diminished at longer time intervals [26-28]. FDG-PET-occult mediastinal nodal metastases are more likely to occur in the setting of central tumors, upper lobe tumors, higher T stage, adenocarcinoma histology, higher standardized uptake value of the primary tumor, and N1 disease [13,29,30].

FDG-PET has sensitivity of 94% and specificity of 82% for characterization of adrenal nodules and is superior to CT alone. Lack of FDG uptake in an adrenal nodule is considered conclusive for benign adrenal adenoma and obviates further workup [31]. Patients with an FDG-avid adrenal nodule as

the only site of potential metastatic disease require biopsy confirmation [11].

The sensitivity, specificity, accuracy, and negative predictive value of FDG-PET for bone metastases are >90%, which is superior to bone scintigraphy [32-35].

Liver metastases may be present in up to 3% to 4% of asymptomatic NSCLC patients at the time of presentation [36]. Although there is heterogeneous physiologic FDG activity in the liver, the accuracy of FDG-PET and PET/CT for liver metastases is reported to be 92% to 100% [37]. When findings are discordant or indeterminate, MRI and/or biopsy are appropriate strategies to evaluate liver lesions.

FDG-PET cannot be used for tumor measurement purposes, but integrated PET/CT allows anatomic measurement on the CT portion of the examination for the T descriptor.

Variant 1: Noninvasive initial clinical staging of non–small-cell lung carcinoma.

C. CT Abdomen and Pelvis

CT abdomen and pelvis with oral and IV contrast may be used as an alternate imaging modality to evaluate for extrathoracic metastasis in lung cancer patients being considered for curative therapy if FDG-PET or PET/CT is not performed [11]. Acquisitions of arterial and portal venous phase sequences are advised.

CT abdomen and pelvis with oral and IV contrast is recommended in NSCLC patients with abnormal clinical evaluation, including signs or symptoms referable to the abdomen and pelvis and no suspicious extrathoracic findings on chest CT [11].

All NSCLC with locally advanced stage III or stage IV disease should undergo extrathoracic imaging with either CT abdomen and pelvis or FDG-PET or PET/CT because of the likelihood of occult extrathoracic metastatic disease in up to 37% of cases [11].

Variant 1: Noninvasive initial clinical staging of non–small-cell lung carcinoma.

D. Bone Scan Whole Body

Technetium-99m (Tc-99m) bone scintigraphy may be used as an alternate imaging modality to evaluate for bone metastasis in NSCLC patients if FDG-PET or PET/CT is not performed or is equivocal for osseous findings.

Bone scintigraphy was historically used to detect osseous metastatic disease in lung cancer patients. A recent meta-analysis found it has a pooled sensitivity of 91.8%; however, the pooled specificity for bone metastases from lung cancer on bone scintigraphy was 68.8%, which is primarily due to confounders such as degenerative disease, inflammation, and prior trauma [38]. FDG-PET and PET/CT have significantly higher sensitivity, specificity, accuracy, and negative predictive value than bone scan [34,35].

Variant 1: Noninvasive initial clinical staging of non–small-cell lung carcinoma.

E. MRI Brain

MRI brain without and with IV contrast is recommended in any patient with clinical stage II, III, or IV NSCLC, even in the absence of neurologic symptoms [39]. MRI brain without and with IV contrast is optional in patients with clinical stage IB NSCLC without neurologic symptoms [39]. MRI brain without and with IV contrast is recommended in all NSCLC patients with neurologic

symptoms, regardless of stage.

MRI brain is the preferred imaging modality for evaluation of intracranial metastases, as it is more sensitive for small brain lesions than CT [11,40]. In a meta-analysis of NSCLC patients without neurologic symptoms, the median prevalence of brain lesions was 3% [11]. However, a small study found that 22% of asymptomatic patients with tumor size >3 cm had brain metastases [41]. Any NSCLC patient with neurologic symptoms should be screened for intracranial metastasis [11]. Brain metastases have been associated with adenocarcinoma NSCLC and N2 disease [11,42].

Variant 1: Noninvasive initial clinical staging of non–small-cell lung carcinoma.

F. CT Head

CT head with IV contrast can be used as an alternate imaging modality in stage III or IV NSCLC patients and NSCLC patients with neurologic symptoms if MRI head is not obtained. Dual-phase imaging may be useful in this clinical setting.

CT scanning of the brain is an appropriate method of evaluating for brain metastases in patients with NSCLC [11]. Although MRI has greater sensitivity than CT, the identification of more and smaller brain lesions on MRI compared with CT has not been associated with better survival or the identification of more patients with brain lesions [43,44].

Variant 1: Noninvasive initial clinical staging of non–small-cell lung carcinoma.

G. MRI Chest

MRI chest without and with IV contrast may be indicated in specific clinical circumstances in NSCLC patients with equivocal findings on CT chest. Focused MRI of the chest may be useful in assessment of chest wall or spinal invasion and tumor involvement of mediastinal structures, including the heart, great vessels, and pericardium. MRI assessment of superior sulcus tumors for brachial plexus involvement is standard of care [45]. MRI is superior to CT for detecting involvement of the neural foramina and spinal canal. Dynamic cine MRI with free breathing can determine lack of invasion if there is respiration-coordinated sliding between the tumor and mediastinum or chest wall, and it can also evaluate for phrenic nerve involvement by lymphadenopathy or the primary tumor.

Conversely, restriction of tumor motion is not conclusive since inflammation or adhesion may also affect mobility [46,47]. MRI is also capable of distinguishing an obstructing tumor from postobstructive atelectasis. Diffusion-weighted imaging (DWI) has been shown to be equal to PET/CT in differentiation of tumor and atelectasis. In the same study, T2-weighted imaging was accurate in 76% of cases [48].

Variant 1: Noninvasive initial clinical staging of non–small-cell lung carcinoma.

H. MRI Abdomen

MRI abdomen with chemical shift sequencing may be used to characterize adrenal nodules when findings on CT chest or CT abdomen are equivocal and FDG-PET or PET/CT is not performed. Indeterminate adrenal nodules may be characterized by chemical shift of in- and out-of-phase MRI to assess for the presence of small intracytoplasmic lipid volume in lipid-poor adenomas. Use of MRI for this purpose is declining because of the high sensitivity and accuracy of PET/CT in identifying adrenal metastases from lung cancer [31].

MRI abdomen with IV contrast may be used to identify small metastatic lesions in the liver when

findings are equivocal on CT chest, CT abdomen, FDG-PET, or PET/CT. MRI abdomen with IV contrast has a higher sensitivity than CT, FDG-PET, or PET/CT for detection and characterization of small liver lesions and may be used for more definitive characterization [49].

Variant 1: Noninvasive initial clinical staging of non–small-cell lung carcinoma.

I. Radiography Chest

Chest radiography is not sufficient for staging of NSCLC.

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

SCLC is an aggressive form of primary pulmonary neuroendocrine tumor with short doubling time and tendency toward early metastasis [50]. The eighth edition of the TNM staging criteria of the American Joint Committee on Cancer applies to patients with SCLC. The TNM staging criteria is recommended to be used in conjunction with the modified Veterans Administration Lung Study Group (VALSG) classification system distinguishing limited stage (LS) from extensive stage (ES) SCLC because of the ongoing use of the VALSG 2-stage classification system in general clinical practice and clinical trials [51-53]. The 5-year overall survival for LS-SCLC is 20% to 25%, while 5-year survival for ES-SCLC approaches zero [51].

The eighth edition of the TNM criteria of the American Joint Committee on Cancer was developed under the auspices of the International Association for the Study of Lung Cancer and informed by database analysis of nearly 95,000 patients primarily from Europe and Asia [4]. Clinical noninvasive staging by radiologic imaging is the first step in determining the appropriate management for patients with SCLC.

T Descriptor

The T descriptor is based on size and location of the primary tumor, the presence or absence of atelectasis or postobstructive pneumonitis, and the degree of invasion into adjacent structures exhibited by the primary tumor [5,6].

- T0 describes no evidence of a primary lung tumor [5].
- T1 comprises tumors up to 3 cm in greatest dimension, subdivided into 3 categories: (1) T1a are tumors ≤ 1 cm; (2) T1b tumors are >1 cm to 2 cm; and (3) T1c are tumors >2 cm to 3 cm [5].
- T2 tumors are 3 to 5 cm, with T2a categorized as tumors >3 cm to 4 cm, while T2b tumors are >4 cm to 5 cm. T2 tumors may be with or without visceral pleural invasion. Other features that pertain to T2 include atelectasis or obstructive pneumonitis extending to the hilum and endobronchial tumors involving a main bronchus any distance from the carina but without carinal involvement [5].
- T3 tumors are >5 cm to 7 cm in size. In addition, ipsilateral satellite nodule in the same lobe as the primary tumor is considered T3 disease. Invasion of the chest wall, phrenic nerve, parietal pleura, or pericardium are also T3 [5].
- T4 tumors are those >7 cm or those which invade the carina, diaphragm, vertebral bod(ies), or mediastinal structures including heart, trachea, esophagus, and recurrent laryngeal nerve. Ipsilateral satellite nodules in a different lobe from the primary tumor signify T4 lesions [5].

N Descriptor

In the eighth edition, the N stage is based on location of metastatic nodes. Increasing number of

involved nodal stations negatively affects prognosis [5]. A lymph node size threshold of > 10 mm in axial short axis diameter is considered abnormal. The prevalence of metastatic lung cancer in thoracic lymph nodes is 30% for nodes that are 10 to 15 mm in short axis diameter and 67% for nodes > 15 mm [5].

- Nx indicates that lymph nodes cannot be assessed [5].
- N0 is consistent with lack of regional node involvement [5].
- N1 includes ipsilateral peribronchial, hilar, or intrapulmonary lymph node(s) [5].
- N2 describes ipsilateral mediastinal or subcarinal lymph node(s) [5].
- N3 includes contralateral mediastinal or hilar lymph node(s) and any supraclavicular or scalene node on either side [5].

M Descriptor

The presence of metastatic lung cancer lesions constitutes stage IV disease. Many patients with SCLC present with metastatic disease [9], and the treatment of stage IV cancers depends on the location and number of lesions.

- M0 disease is consistent with no distant metastases [5].

The M1 classification is subdivided into three categories:

- M1a includes satellite nodule(s) in the contralateral lung and cytology proven malignant pleural or pericardial effusion [5].
- M1b indicates a single extrathoracic metastasis. This category also includes metastasis in a single nonregional lymph node, considered nodes not in the N descriptor, such as axillary, internal mammary, or abdominal lymph node(s) [5,6].
- M1c indicates multiple extrathoracic metastases in one or more organs [5].

Modified VALSG Staging

Under the modified VALSG staging classification, SCLC is considered LS disease when it is confined to a single hemithorax (although local extension may be present); the primary tumor and regional nodes can be addressed by a single radiation port; and ipsilateral supraclavicular nodes can be included in the same radiation field as the primary tumor. Contralateral mediastinal lymph nodes and ipsilateral pleural effusion are also considered LS-SCLC [51,52].

ES-SCLC includes disease that is not confined to a single radiation port, malignant pericardial effusion, contralateral pleural effusion, and distant hematogenous metastases [51,52].

The classification of contralateral supraclavicular or hilar lymph nodes is controversial. These nodes should be assessed on a case-by-case basis as to whether they may be feasibly included within a single radiation port [51,52].

In the combined TNM/VALSG approach for staging of SCLC, T1 and T2 lesions and M1a ipsilateral pleural disease correspond with LS-SCLC. T3 and T4 lesions are conditional and may be LS or ES depending on the feasibility of inclusion within a single radiation port. Other M descriptors, including M1a contralateral pleural effusion, M1a pericardial effusion, M1b, and M1c comprise ES-SCLC [54].

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

A. CT Chest

For patients with known or suspected SCLC, chest CT with IV contrast is recommended. If concurrent CT abdomen is not obtained, the adrenal glands should be covered. Chest CT without IV contrast may also be used.

Chest CT is the modality of choice for initial evaluation of the SCLC. A large percentage of SCLCs arise from the central lobar or main bronchi. Consequently, the most common appearance of SCLC on imaging studies is a centrally located lung mass or mediastinal mass with hilar involvement [50]. In two-thirds of patients, tumor tissue encases mediastinal structures, including vessels, airways, and the esophagus [50]. Diagnosis of chest wall invasion on CT can be equivocal in cases of minimal invasion. Radiologic imaging cannot dependably detect visceral pleural invasion.

Chest CT with IV contrast can aid in the identification of chest wall invasion by tumor, assessment of extent of mediastinal invasion, evaluation of additional mediastinal and hilar lymph nodes, distinction of central obstructing tumor from surrounding atelectasis, and assessment for liver metastases [50,51]. Unenhanced CT may be better able to characterize adrenal nodules.

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

B. CT Abdomen and Pelvis

CT abdomen and pelvis with oral and IV contrast is recommended in conjunction with CT chest to evaluate for extrathoracic metastasis in SCLC patients. Acquisition of arterial and portal venous phase sequences is advised. CT abdomen without IV contrast may also be obtained. Dual-phase imaging may be useful in this clinical setting.

Up to 60% of SCLC patients have metastases to the abdominal organs at presentation. The liver and adrenal gland are the most frequent site of hematogenous metastasis [55]. Traditionally, CT abdomen with IV contrast has been used to evaluate for extrathoracic metastases and distinguish between LS-SCLC and ES-SCLC. FDG-PET or PET/CT is increasingly used for this purpose and usually obviates the need for a separate CT abdomen and pelvis examination.

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

C. FDG-PET/CT Skull Base to Mid-Thigh

FDG-PET or PET/CT is recommended in patients with clinical stage I or II LS-SCLC being considered for treatment with curative intent. FDG-PET or PET/CT for further staging is optional if ES-SCLC is established.

FDG-PET has been shown on average to upstage the disease in up to 18% of patients with clinical LS-SCLC by conventional imaging. A meta-analysis of 7 prospective and retrospective trials found changes in management based on PET findings in 24% to 47% of SCLC patients [52,56,57]. A FDG-PET scan has superior sensitivity and specificity compared with CT in identification of metastatic disease other than brain metastases in SCLC patients [58-60].

Up to 60% of SCLC patients have metastases to the abdominal organs. The liver and adrenal gland are the most frequent site of hematogenous metastasis [55]. Although there is heterogeneous physiologic FDG activity in the liver, the accuracy of FDG-PET and PET/CT for liver metastases is reported at 92% to 100% [37]. When findings are discordant or indeterminate, MRI or biopsy are appropriate strategies to evaluate liver lesions. FDG-PET has sensitivity of 94% and specificity of

82% for characterization of adrenal nodules and is superior to CT alone. Lack of FDG uptake in an adrenal nodule is considered conclusive for benign adrenal adenoma and obviates further workup [31]. Patients with an FDG-avid adrenal nodule as the only site of potential metastatic disease require biopsy confirmation [51].

The sensitivity, specificity, accuracy, and negative predictive value of FDG-PET for bone metastases is greater than 90% and is superior to bone scintigraphy [33,34].

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

D. MRI Brain

MRI brain with IV contrast is recommended in all SCLC patients. MRI brain identifies metastatic lesions in 10% to 15% of newly diagnosed SCLC patients without neurologic symptoms. Up to 12% of patients with otherwise LS-SCLC have intracranial metastases on MRI [61]. MRI is more sensitive than CT for detection of intracranial metastases. MRI brain without IV contrast may be performed.

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

E. CT Head

CT head with IV contrast can be used as an alternate imaging modality in SCLC patients if brain MRI is not performed. Although MRI has greater sensitivity for small brain metastases, CT scanning of the brain is an appropriate method of evaluating for brain metastases in patients with SCLC [51].

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

F. Bone Scan Whole Body

Tc-99m bone scintigraphy may be used as an alternate imaging modality to evaluate for extrathoracic bone metastasis in SCLC patients if FDG-PET or PET/CT is not performed. Bone metastases are present at the time of diagnosis in up to 37% of SCLCs and are a poor prognostic factor [62,63]. Historically, bone scintigraphy was indicated for the workup of all SCLC patients, but FDG-PET and PET/CT have largely replaced it [51].

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

G. MRI Chest

MRI chest without and with IV contrast may be indicated in specific clinical circumstances in SCLC patients with equivocal findings on CT chest. Focused MRI of the chest may be useful in assessment of chest wall or spinal invasion and tumor involvement of mediastinal structures including the heart, great vessels, or pericardium. SCLC of the superior sulcus is less common than NSCLC [64] but requires MRI evaluation for locoregional disease affecting the brachial plexus [45]. MRI is superior to CT for detecting involvement of the neural foramina and spinal canal. Dynamic cine MRI with free breathing can determine lack of invasion if there is respiration-coordinated sliding between the tumor and mediastinum or chest wall. Conversely, restriction of tumor motion is not conclusive since inflammation or adhesion may also affect mobility [46,47]. MRI is also capable of distinguishing an obstructing tumor from postobstructive atelectasis. DWI has been shown to be equal to PET/CT in differentiation of tumor and atelectasis. In the same study, T2-weighted imaging was accurate in 76% of cases [48].

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

H. MRI Abdomen

MRI abdomen with chemical shift sequencing may be used to characterize adrenal nodules when findings are equivocal on CT chest or CT abdomen and FDG-PET or PET/CT is not performed. MRI abdomen with IV contrast may be used to identify small metastatic lesions in the liver when

findings are equivocal on CT chest or CT abdomen or FDG-PET or PET/CT.

Indeterminate adrenal nodules may be characterized by chemical shift of in- and out-of-phase MRI to assess for the presence of small intracytoplasmic lipid volume in lipid-poor adenomas. Use of MRI for this purpose is declining because of the high sensitivity and accuracy of PET/CT in identifying adrenal metastases from lung cancer [31].

MRI abdomen with IV contrast has a higher sensitivity than CT, FDG-PET, or PET/CT for detection and characterization of small liver lesions and may be used for more definitive characterization [49].

Variant 2: Noninvasive initial clinical staging of small-cell lung carcinoma.

I. Radiography Chest

Chest radiography is not sufficient for staging of SCLC.

Summary of Highlights

- **Variant 1:** CT chest with IV contrast or CT chest without IV contrast is usually appropriate for the noninvasive initial clinical staging of NSCLC. These procedures are equivalent alternatives. FDG-PET/CT is usually appropriate to evaluate for extrathoracic metastases in patients with NSCLC. FDG-PET/CT is not required for patients with stage 0 adenocarcinoma in situ with an otherwise normal chest CT examination. MRI head without and with IV contrast is usually appropriate in any patient with clinical stage II, III, or IV NSCLC, even in the absence of neurologic symptoms. MRI head without and with IV contrast is optional in patients with clinical stage IB NSCLC without neurologic symptoms. MRI head without and with IV contrast is recommended in all NSCLC patients exhibiting neurologic symptoms, regardless of stage.
- **Variant 2:** CT chest with IV contrast and MRI head without and with IV contrast even in the absence of neurological symptoms are usually appropriate for the noninvasive initial clinical staging of SCLC. FDG-PET/CT skull base to mid-thigh or CT abdomen and pelvis with IV contrast is usually appropriate; however, FDG-PET/CT is more sensitive for lymph node and adrenal metastases, and it is superior to CT for bone marrow metastases.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at <https://acsearch.acr.org/list>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at <https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria>.

Appropriateness Category Names and Definitions






| Appropriateness Category Name | Appropriateness Rating | Appropriateness Category Definition |
|--------------------------------------|-------------------------------|--|
| Usually Appropriate | 7, 8, or 9 | The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk- |

| | | |
|-----------------------------------|------------|--|
| | | benefit ratio for patients. |
| May Be Appropriate | 4, 5, or 6 | The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal. |
| May Be Appropriate (Disagreement) | 5 | The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned. |
| Usually Not Appropriate | 1, 2, or 3 | The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable. |

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations

| Relative Radiation Level* | Adult Effective Dose Estimate Range | Pediatric Effective Dose Estimate Range |
|---|-------------------------------------|---|
| 0 | 0 mSv | 0 mSv |
|  | <0.1 mSv | <0.03 mSv |
|  | 0.1-1 mSv | 0.03-0.3 mSv |
|  | 1-10 mSv | 0.3-3 mSv |
|  | 10-30 mSv | 3-10 mSv |
|  | 30-100 mSv | 10-30 mSv |

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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Disclaimer

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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