American College of Radiology
ACR Appropriateness Criteria®
Lung Cancer: Surveillance After Therapy

Variant: 1 Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.

Procedure	Appropriateness Category	Relative Radiation Level
CT chest with IV contrast	Usually Appropriate	☢☢☢
CT chest without IV contrast	May Be Appropriate (Disagreement)	☢☢☢
Radiography chest	Usually Not Appropriate	☢
MRI chest without and with IV contrast	Usually Not Appropriate	O
MRI chest without IV contrast	Usually Not Appropriate	O
MRI head without and with IV contrast	Usually Not Appropriate	O
MRI head without IV contrast	Usually Not Appropriate	O
Bone scan whole body	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢
CT head with IV contrast	Usually Not Appropriate	☢☢☢
CT head without and with IV contrast	Usually Not Appropriate	☢☢☢
CT head without IV contrast	Usually Not Appropriate	☢☢☢
CT neck with IV contrast	Usually Not Appropriate	☢☢☢
CT neck without and with IV contrast	Usually Not Appropriate	☢☢☢
CT neck without IV contrast	Usually Not Appropriate	☢☢☢
CTA chest with IV contrast	Usually Not Appropriate	☢☢☢
CTA chest without and with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT chest abdomen pelvis with IV contrast	Usually Not Appropriate	☢☢☢☢
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	☢☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

Variant: 2 Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.

Procedure	Appropriateness Category	Relative Radiation Level
MRI head without and with IV contrast	Usually Appropriate	O
MRI head without IV contrast	Usually Appropriate	O
CT chest with IV contrast	Usually Appropriate	☢☢☢
CT chest abdomen pelvis with IV contrast	May Be Appropriate	☢☢☢☢
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	☢☢☢☢
Radiography chest	Usually Not Appropriate	☢
MRI chest without and with IV contrast	Usually Not Appropriate	O
MRI chest without IV contrast	Usually Not Appropriate	O

Bone scan whole body	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢
CT chest without IV contrast	Usually Not Appropriate	☢☢☢
CT head with IV contrast	Usually Not Appropriate	☢☢☢
CT head without and with IV contrast	Usually Not Appropriate	☢☢☢
CT head without IV contrast	Usually Not Appropriate	☢☢☢
CT neck with IV contrast	Usually Not Appropriate	☢☢☢
CT neck without and with IV contrast	Usually Not Appropriate	☢☢☢
CT neck without IV contrast	Usually Not Appropriate	☢☢☢
CTA chest with IV contrast	Usually Not Appropriate	☢☢☢
CTA chest without and with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	☢☢☢☢

Variant: 3 Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.

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

<u>Variant: 4</u> Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.

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

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Summary of Literature Review

Introduction/Background

The lifetime risk of lung cancer in the United States is 6.1% for an average-risk individual, and the mortality from lung cancer is greater than that of breast, prostate, and colon cancer combined [1]. Fortunately, there has been a decline in the incidence and mortality of lung cancer in the United States over the last 2 decades paralleling a decline in smoking [2], however, the burden of disease is still significant because the incidence of lung cancer continues to increase in Asia. Most lung cancer statistics include both non–small-cell lung cancer (NSCLC) representing 80% to 85% of lung

cancers and small-cell lung cancer (SCLC) comprising the remaining 10% to 15% of all lung cancers.

Evidence-based surveillance for patients with lung cancer is of critical importance for early detection of potentially salvageable recurrence. The detection of disease recurrence or secondary primary lung cancer (SPLC) in patients with lung cancer treated with curative intent is important for patients' survival outcomes. Multiple posttreatment surveillance guidelines are available from national and international oncologic societies, including the National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology (ASCO), the American College of Chest Physicians (ACCP), and the European Society for Medical Oncology (ESMO). Owing to a lack of high-quality data on surveillance imaging of asymptomatic patients with lung cancer, these guidelines are mainly based on lower-level evidence and expert opinion, sometimes with varying recommendations. There is controversy regarding the imaging modality, frequency, and duration of follow-up [3-5]. The treatment modality (surgery versus radiotherapy) impacts timing of follow-up chest CT scans. For instance, per the current NCCN and ASCO guidelines, recommendations are for chest CT every 6 months for 2 years after surgery and then moving on to annual low-dose screening CT, however, if the primary treatment included radiation, the recommendation is for CT chest every 3 to 6 months for 3 years after radiotherapy before moving onto low-dose annual screening CT after 5 years [5,6].

For the purposes of this review, curative-intent treatment for a patient with stage I-III NSCLC was defined as surgical resection with or without adjuvant therapy, stereotactic or radical radiotherapy, or chemoradiotherapy. Conversely, only one-third of patients with SCLC present with limited-stage disease (I-III) for which the curative-intent standard of care is usually chemotherapy and concurrent radiotherapy, followed by prophylactic cranial irradiation (PCI) if indicated. The current review does not address surveillance after attempted definitive therapy for oligometastatic disease as treatment of oligometastatic disease would be considered palliative.

Discussion of other thoracic malignancies such as carcinoid, thymoma, or mesothelioma is beyond the scope of this topic.

Discussion of Procedures by Variant

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.

Routine surveillance strategies pertain only to patients with curatively treated stage I-III NSCLC with no clinical suspicion of recurrent disease. Additionally, some patients with stage IV NSCLC may go into remission and are often managed similar to other patients with stage I-III disease with regards to imaging follow-up. This includes patients treated with surgery, stereotactic body radiotherapy, and chemoradiation. Imaging to evaluate symptoms and follow-up on previous findings is not included within the purview of routine surveillance imaging. In addition, if the patient is clinically unsuitable and unwilling to accept further treatment, surveillance imaging may be omitted because most surveillance is done to assess for local recurrence that might be definitively treated.

In one of the largest meta-analyses by Stirling et al [7], a total of 13 studies (5,759 patients) were identified, in which a prospective surveillance strategy was identifiable for surveillance of NSCLC

after curative-intent treatment. There was considerable heterogeneity in the surveillance modalities and frequency/timing of the surveillance, including history and physical examination, biochemistry, tumor markers, sputum cytology, chest radiograph, CT, PET/CT, MRI, bone scintigraphy, and bronchoscopy. Intended duration of follow-up in these studies varied from 2 years [8], 5 years [9], ongoing [10], or undefined. Confirmation of recurrences was variably reported and documented after biopsy and histologic confirmation, radiologic or PET suspicion, or radiologic or PET size progression before treatment or regression after retreatment.

The recommended long-term surveillance workup in patients with NSCLC is based on the tumor stage and primary treatment modality and imaging guidelines provided by different societies differs mostly with respect to the timing and duration of scans [3-5].

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
A. Bone scan whole body

There is no relevant literature to support the use of whole-body bone scintigraphy for noninvasive imaging surveillance of NSCLC treated with curative intent.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
B. CT abdomen and pelvis with IV contrast

For patients with stage I-III NSCLC treated with curative-intent and with no clinical suspicion of recurrent disease, the NCCN and ASCO guidelines recommend that patients should undergo a diagnostic chest CT including the adrenal glands (preferably done with intravenous [IV] contrast). There is no evidence of added benefit for a CT of the abdomen and pelvis with IV contrast over a chest CT through the adrenals as a surveillance imaging modality for recurrence [3,5].

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
C. CT abdomen and pelvis without and with IV contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast for imaging surveillance of patients with curatively treated NSCLC. For patients with stage I-III NSCLC treated with curative intent and with no clinical suspicion of recurrent disease, the NCCN and ASCO guidelines recommend that patients should undergo a diagnostic chest CT including the adrenal glands (preferably done with IV contrast) [3,5].

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
D. CT abdomen and pelvis without IV contrast

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast for imaging surveillance of patients with curatively treated NSCLC. For patients with stage I-III NSCLC treated with curative-intent and with no clinical suspicion of recurrent disease, the NCCN and ASCO guidelines recommend that patients should undergo a diagnostic chest CT including the adrenal glands (preferably done with IV contrast) [3,5].

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
E. CT chest abdomen pelvis with IV contrast

Per the ASCO guidelines [5], there was no evidence of added benefit for a CT of the abdomen and

pelvis over a chest CT through the adrenals as a surveillance imaging modality for recurrence. Hence, there is scant literature regarding the use of combined chest and abdominal imaging for surveillance of curatively treated NSCLC.
In the French IFCT-0302 trial, including 1,775 patients with completely resected lung cancer (stage I-IIIA), 2 different follow-up strategies were evaluated: clinical examination and chest radiography (control arm) versus a combination of clinical examination, chest radiography, chest and abdominal CT scan (not mentioned if with IV contrast), plus bronchoscopy (experimental arm). After a median follow-up of 8.7 years, no significant difference in overall survival (OS) was observed in the 2 groups (hazard ratio [HR] 0.92, 95% confidence interval [CI], 0.8-1.07, P = .27). Disease-free survival rates at 3 years were 63.3% and 60.2% in the experimental arm and the control arm, respectively. The 8-year OS rates were 55.6% and 51.1%, respectively (95% CI, 51.7%-59.4%). The authors concluded no significant survival benefit was identified with the addition of CT [11]. Although the benefit to OS is not statistically significant, there is a trend toward use of CT for surveillance because some benefit maybe derived from early detection of second primary lung malignancy in these patients.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
F. CT chest abdomen pelvis without and with IV contrast

Per the ASCO and NCCN guidelines, there is no evidence of added benefit for a CT of the abdomen and pelvis over a chest CT through the adrenals as a surveillance imaging modality. There is no relevant literature to support the use of CT chest abdomen and pelvis without and with IV contrast for imaging surveillance of patients with curatively treated NSCLC [3,5].

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
G. CT chest abdomen pelvis without IV contrast

Per the ASCO and NCCN guidelines, there is no evidence of added benefit for a CT of the abdomen and pelvis over a chest CT through the adrenals as a surveillance imaging modality. There are no specific studies comparing CT chest abdomen pelvis with IV contrast with those comparing CT chest, abdomen, and pelvis without IV contrast for routine surveillance imaging of patients with lung cancer treated with curative intent [3,5].

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
H. CT chest with IV contrast

The aim of posttreatment surveillance is the detection of treatment-related complications, tumor recurrences, and/or SPLC [12]. There is consensus regarding the imaging modality used for surveillance, and most societies recommend a CT chest preferably with IV contrast, however, there is poor consensus regarding timing of surveillance chest CT. For instance, the ACCP guidelines recommend performing chest CT scans every 6 months for the first 2 years after resection [13], whereas the NCCN recommends a chest CT with or without IV contrast every 6 months for 2 to 3 years. The ESMO guidelines for early and locally advanced NSCLC also acknowledge the low level of evidence regarding the benefit of surveillance following curative-intent therapy and recommends an annual or biannual chest CT [14].

Efforts to establish evidence to support a specific modality and frequency for surveillance imaging have led to multiple small retrospective studies with conflicting results. As mentioned above, only 1

prospective trial, the IFCT-0302, randomized patients to every 6 months CT examination, and chest radiography (with or without bronchoscopy) to examination and chest radiography alone. At a median follow-up of 8.7 years, no significant survival benefit was identified with the addition of CT, although longer follow-up is ongoing [11]. Although the difference in survival was not statistically significant, there is a trend of increasing use of CT for imaging surveillance due to its ability to detect a second primary lung malignancy early. Therefore, a longer follow-up interval has been noted, from 3 years to 8 years follow-up in some studies. Lou et al [15] reported their experience with the role of chest CT in the follow-up of patients with surgically treated lung cancer and found that recurrence and SPLC were diagnosed in 20% and 7% of patients, respectively. The majority of new primary cancers (93%) were identified by scheduled routine CT scan, as were a smaller majority of recurrences (61%). During the first 4 years after surgery, the risk of recurrence ranged from 6% to 10% per person-year but decreased thereafter to 2%. Conversely, the risk of SPLC ranged from 3% to 6% per person-year and did not diminish over time.

A systematic review by Srikantharajah et al [16] identified 5 relevant studies that investigated the impact of chest CT surveillance in patients who had undergone surgical resection for NSCLC. The authors found conflicting results, with 3 studies that showed a survival benefit and 2 studies that did not.

Some studies have suggested that the early diagnosis of recurrence might impact OS outcomes or quality of life. A systematic review and meta-analysis found a trend toward better survival in an intensive follow-up program, similar to the abovementioned French study, and the identification of recurrence in asymptomatic patients was associated with significantly increased survival [17]. Asymptomatic recurrences had significantly better survival rates than symptomatic recurrences; a majority of the recurrences that could be treated with curative intent were diagnosed by chest CT, and systematic follow-up of NSCLC not only detected local recurrence but also detected an SPLC at an early stage (IA) that was potentially resectable.

In patients with stage III unresectable disease who have undergone chemoradiation, use of contrast-enhanced CT is recommended over unenhanced CT because the former offers greater accuracy and reduced interreader variability in the identification of hilar lymph nodes, as well as reliable detection of mediastinal lymph nodes and abdominal progression [18].

However, adrenal nodules may not be definitively characterized by CT if IV contrast is used and may benefit from further characterization with PET/CT, MRI abdomen, or adrenal washout CT [19].

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
I. CT chest without and with IV contrast

There is no relevant literature to support the use of CT chest without and with IV contrast for imaging surveillance of patients with curatively treated NSCLC.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
J. CT chest without IV contrast

An adequate interpretation of posttreatment radiologic examinations is based on the understanding of the performed surgical intervention and treatment history including stereotactic body radiation therapy and chemotherapy or immunotherapy. Chest CT with IV contrast is

recommended over noncontrast CT of the chest to identify mediastinal/hilar and abdominal disease progression. Noncontrast chest CT, however, is adequate for the identification of new ipsilateral or contralateral lung nodules. It also identifies pleural or pericardial effusions that may need cytological confirmation as site of disease if pleural or pericardial nodules are not visible. Differentiating recurrence from postsurgical changes (such as atelectasis or muscle flaps) may be challenging on noncontrast CT. A soft tissue nodule near the surgical clips may represent either granulation tissue or tumor recurrence. On follow-up with serial CT scans, the interval growth of solid or subsolid nodule close to the staple line is suggestive of recurrence [20].

Osseous metastases and extra thoracic metastasis involving the adrenal glands may also be delineated quite well on a noncontrast chest CT, however, adrenal nodules may not be definitively characterized by CT if intracytoplasmic lipid content is low, which occurs in approximately one-third of adrenal adenomas.

Two or more years after curative-intent therapy, patients are at higher risk of developing an SPLC (1.5%-2% per year) and may benefit from a screening approach similar to that offered to those who meet the National Lung Screening Trial eligibility. A low-dose noncontrast chest CT scan affords good imaging quality with lower doses of radiation (approximately 2 mSv). Patients with a prior history of lung cancer have a higher risk of a new primary lung cancer than the at-risk population defined in the National Lung Screening Trial. Clinicians should use a low-dose screening chest CT when conducting surveillance for new lung primaries after the first 2 years posttreatment [5].

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
K. CT head with IV contrast

Surveillance to detect distant metastasis in the brain, bone, or other distant sites has not been found to improve survival because metastatic recurrences are incurable by definition. Per the NCCN and ASCO guidelines [3,5], imaging of the brain with MRI or CT is not recommended as a surveillance tool in patients with curatively treated stage I-III NSCLC, Although MRI has greater sensitivity than CT, identification of a greater number and smaller brain lesions on MRI compared with CT has not been associated with better survival.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
L. CT head without and with IV contrast

There is no relevant literature to support the use of CT head without and with IV contrast for imaging surveillance of patients with curatively treated NSCLC.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
M. CT head without IV contrast

There is no relevant literature to support the use of CT head without IV contrast for imaging surveillance of patients with curatively treated NSCLC.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
N. CT neck with IV contrast

There is no relevant literature to support the use of CT neck with IV contrast for routine surveillance imaging of patients with lung cancer treated with curative intent.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
O. CT neck without and with IV contrast

There is no relevant literature to support the use of CT neck without and with IV contrast for routine surveillance imaging of patients with lung cancer treated with curative intent.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
P. CT neck without IV contrast

There is no relevant literature to support the use of CT neck without IV contrast for routine surveillance imaging of patients with lung cancer treated with curative intent.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
Q. CTA chest with IV contrast

Pulmonary thromboembolism is common in patients with lung cancer and incidence is increased by surgery, chemotherapy, radiotherapy, and disease progression. Although CTA of the chest with IV contrast can frequently detect recurrence, it is typically reserved for patients with symptoms suggestive of pulmonary embolism and is not commonly used for routine surveillance.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
R. CTA chest without and with IV contrast

There is no relevant literature to support the use of CTA chest without and with IV contrast for routine surveillance imaging of patients with lung cancer treated with curative intent.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
S. FDG-PET/CT skull base to mid-thigh

There is still substantial debate over the optimal frequency, timing, and imaging modalities for early posttreatment and long-term surveillance of patients with lung cancer, particularly those treated with curative-intent therapy.

Several studies showed that FDG-PET/CT has superior performance for recurrence detection in patients with NSCLC who underwent potentially curative surgery, compared with conventional CT. For instance, in a prospective study by Choi et al [21], 358 patients with NSCLC who underwent curative tumor resection were followed with IV contrast-enhanced chest CT at 6-month intervals and FDG-PET/CT annually for 5 years. Recurrent disease occurred in 31% of patients; recurrence was detected with both CT and FDG-PET/CT in 51% and only with FDG-PET/CT in 37% of cases, however, ground-glass lesions and small adenocarcinomas were often missed by FDG-PET. Five lung lesions and 1 pancreatic metastasis were detected with chest CT only. Some studies have demonstrated that asymptomatic patients with recurrences detected by intensive surveillance had a better prognosis than symptomatic patients [22]. Toba et al [23] reported high values of sensitivity (94.4%) and specificity (97.6%) for the detection of recurrences with FDG-PET/CT in asymptomatic patients with NSCLC after a potentially curative operation. Considering that most recurrences occurred during the initial 2 years after surgery, the authors suggested examining the

whole body with FDG-PET/CT periodically during this time.

A few studies have also suggested the benefit of early posttreatment surveillance FDG-PET/CT for the detection of recurrence in patients with NSCLC who were treated with curative-intent radiotherapy and chemotherapy. In a prospective study of 100 patients with NSCLC, van Loon et al [24] showed that FDG-PET/CT 3 months after radical radiotherapy could identify progression amenable for curative treatment in 3% of patients, all of whom were asymptomatic. Early detection of locoregional or potentially salvageable recurrences can potentially prolong the OS in patients with early-stage NSCLC who were treated with definitive-intent surgical or radiation therapy or those with oligometastatic NSCLC (3 or fewer metastases) who can benefit from local ablative therapies [25,26].

Conversely, a prospective randomized controlled trial led by Gambazzi et al [8] compared the performance of integrated FDG-PET/CT and contrast-enhanced CT and concluded that PET/CT was not superior to contrast-enhanced chest CT in detecting cancer recurrence during 2 years after curative-intent treatment of NSCLC. Takenaka et al [27] prospectively compared diagnostic capabilities of whole body integrated FDG-PET/CT and standard radiologic examination for assessment of recurrence in postoperative patients with NSCLC and found no statistically significant differences between integrated FDG- PET/CT and standard radiologic examinations such as chest CT.

Imaging Following Radiotherapy: One of the challenges of posttreatment assessment is imaging during and after radiotherapy. Radiation is typically used as a curative-intent treatment modality for patients who are deemed medically inoperable and have early-stage NSCLC. In these circumstances, a follow-up FDG-PET/CT is not recommended in the first 3 months to ensure resolution of therapy related FDG uptake. In the post–stereotactic ablative radiotherapy setting, recurrent disease should be suspected if high-risk CT changes are seen with maximum standardized update value (SUVmax) ≥5 on PET, however, in the stereotactic ablative radiotherapy setting, FDG-avidity can also be related to normal acute radiation inflammatory response of lung tumors/parenchyma [4].

Although studies have demonstrated the value of FDG-PET/CT for the detection of postoperative recurrence, in patients with NSCLC, there are no prospective randomized studies showing an OS benefit of using FDG-PET/CT for imaging surveillance compared to routine CT imaging [21,23,28,29].

Therefore, currently, the routine use of FDG-PET/CT is not recommended in lung cancer surveillance and is reserved for cases of suspected relapse and those with inconclusive CT. For patients with stage I-III NSCLC treated with curative intent and with no clinical suspicion of recurrent disease, the NCCN and ASCO guidelines [3,5], recommend that FDG-PET/CT should not be used as a surveillance tool. This includes patients treated with surgery, stereotactic body radiotherapy, and chemoradiation. FDG-PET/CT may be useful for assessing CT findings that are a concern for malignancy but that may alternatively represent radiation fibrosis, atelectasis, or other benign conditions. Due to false-positive findings from postsurgical granulation tissue response and postradiation related inflammation and fibrosis, the detection of local recurrence on FDG-PET/CT can be challenging.

Imaging Following Radiofrequency Ablation: A pattern of focally intense and increasing fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET uptake has high sensitivity and specificity for detecting recurrent lung cancer following radiofrequency ablation (RFA). Surveillance after RFA should include a contrast-enhanced diagnostic CT at 1 month to diagnose procedural complications, PET at 6 months as a posttreatment metabolic baseline (with diagnostic CT if PET is abnormal), and alternating diagnostic CTs or PET every 6 months for 2 years [30]. PET/CT after RFA has a high rate of false-positives in the immediate post-RFA phase (30 days) and initial 6 month period when it can show prominent nonfocal increased uptake in the ablation zone, however, this regresses in the 6- to 12-month period. In this setting, dual-energy CT shows promise in detecting early recurrence post-RFA. In a study by Izaaryene et al [31], the sensitivity of dual-energy CT for detecting lung cancer recurrence at 1 month follow-up after RFA was 100% with a specificity of 85.71% and a negative predictive value (NPV) of 100%.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
T. MRI chest without and with IV contrast

In general, MRI chest is not useful for the routine imaging surveillance in patients with lung cancer. Diffusion-weighted imaging (DWI) can potentially differentiate benign from malignant nodes, which have increased cellularity and less extracellular space [32,33]. Therefore, the diffusion of water in malignant lesions is restricted, resulting in a decreased apparent diffusion coefficient [32,34]. This technique showed lower false-positive findings for NSCLC staging compared with FDG-PET/CT and was highly accurate in distinguishing lymphadenitis from malignant nodes. Further studies are needed to test DWI accuracy for the detection of lung cancer recurrence after surgery, particularly when FDG-PET/CT findings are equivocal.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
U. MRI chest without IV contrast

There is no relevant literature to support the use of MRI chest without IV contrast for routine surveillance imaging of patients with NSCLC treated with curative intent. DWI can potentially differentiate benign from malignant nodes, which have increased cellularity and less extracellular space [32,33]. Therefore, the diffusion of water in malignant lesions is restricted, resulting in a decreased apparent diffusion coefficient [32,34]. This technique showed lower false-positive findings for NSCLC staging compared with FDG-PET/CT and was highly accurate in distinguishing lymphadenitis from malignant nodes. Further studies are needed to test DWI accuracy for the detection of lung cancer recurrence after surgery, particularly when FDG-PET/CT findings are equivocal.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
V. MRI head without and with IV contrast

Per several oncologic guidelines, brain MRI is not useful as a routine surveillance tool in asymptomatic patients with NSCLC who have undergone curative-intent treatment.

The incidence of brain metastases among patients with localized NSCLC ranges from approximately 5% to 40% [35,36]. Although PCI might reduce the incidence of brain metastasis in patients with NSCLC, it does not provide a survival benefit. There have been no randomized trials to date evaluating the use of brain MRI for surveillance in NSCLC, although the usefulness of PCI as

a means to reduce clinically relevant brain metastases and potentially improve the cure rate has been the subject of several randomized trials. Although these trials consistently demonstrated a relative reduction in the incidence of brain metastases by more than 50%, none yielded a survival advantage, and some have revealed neurocognitive decline. Hence, systematic use of brain MRI as a surveillance tool for curatively treated stage I-III NSCLC is discouraged per the ASCO guidelines [5], mainly on the basis of the lack of supporting evidence. Given that PCI has not improved survival or quality of life, routine brain MRI for surveillance in asymptomatic patients is unlikely to provide a meaningful clinical benefit.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
W. MRI head without IV contrast

Per several oncologic guidelines, brain MRI is not useful as a routine surveillance tool in asymptomatic patients with NSCLC who have undergone curative-intent treatment.

Variant 1: Variant 1: Adult. Noninvasive imaging surveillance following treatment of stage I-III non–small-cell lung cancer. Routine surveillance.
X. Radiography chest

In a study by Hanna et al [37], the sensitivity for detection of recurrent disease by chest radiography was low, at 21.2%, and specificity was 91.7%, whereas the sensitivity and specificity by CT where approximately 93% to 94.2% and 86% (range 83.7%-88.1%), respectively [8]. There were no cancers diagnosed on chest radiography that were not detected on minimal dose chest CT. The low sensitivity is multifactorial and likely due to the small size of pulmonary nodules or location close to suture line or metastatic nodal disease involving nodes, in which chest radiography tends to be less well suited. Therefore, chest radiography is not useful for surveillance of patients with NSCLC treated with curative intent.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.

SCLC accounts for approximately 15% of all lung cancer cases and is an aggressive malignancy that is characterized by a rapid doubling time and high growth fraction. Limited-stage SCLC (LS-SCLC) (stages I, II, and sometimes III) is defined as a disease confined to the ipsilateral hemithorax and represents roughly one-third of the cases at diagnosis and is a potentially curable disease with long-term survival of 10% to 15%. Extensive-stage SCLC (ESSCLC) (stage IV) is defined by the presence of tumor extension to the contralateral hemithorax, distant metastases, or T3 or T4 disease with multiple lung nodules or when the tumor/nodal volume does not fit within a tolerable radiation plan. LS-SCLC is typically treated with a combination of chemotherapy and early concurrent thoracic irradiation, whereas ES-SCLC is treated with systemic chemotherapy. PCI may be performed after completion of chemotherapy in patients with LS-SCLC or ES-SCLC who have responded to chemotherapy. Approximately 60% to 70% of patients present with metastatic disease at the time of diagnosis, and the overall prognosis for this group remains poor, however, in patients with LS-SCLC, curative-intent chemoradiation results in a 5-year survival rate of 10% to 15%. [38]. Long-term survival in ES-SCLC is rare, however, systemic chemotherapy with concurrent radiotherapy can prolong survival and improve quality of life [39].

ES-SCLC is more common than LS-SCLC, however, routine surveillance strategies pertain mostly to patients with curatively treated stage I-III SCLC with no clinical suspicion of recurrent disease, comprising approximately one-third of patients with SCLC. A very small percentage of patients

with stage IV SCLC may also go into remission and are often managed similar to other patients with stage I-III disease with regards to imaging follow-up. There is no consensus definition regarding the time frame that differentiates response assessment and surveillance. Imaging to evaluate new symptoms and follow-up on previous findings is not included within the purview of routine surveillance imaging. In addition, if the patient is clinically unsuitable and unwilling to accept further treatment, surveillance imaging may be omitted. The patients age, however, should not preclude surveillance imaging.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
A. Bone scan whole body

Overall, the most common sites of metastases in patients with SCLC are bone (19%-38% of cases), liver (17%-34%), adrenal glands (10%-17%), and brain (up to 14%). Bone metastases are present at the time of diagnosis in up to 37% of patients with SCLC and are a poor prognostic factor [40]. FDG-PET/CT is typically performed initially in patients with SCLC, however, if FDG-PET/CT is unavailable, Tc-99m bone scintigraphy may be used as an alternative initial imaging modality to evaluate for bone metastasis. In a meta-analysis performed by Qu et al [41], bone scintigraphy was unable to detect bone metastasis on the early stage and also unable to differentiate trauma, healing fractures, benign neoplasm, and degenerative disease from metastasis. The sensitivity of bone scan for lung cancer metastasis detection was 86% (95% CI, 0.82-0.89) versus 92% for FDG-PET/CT (95% CI, 0.88-0.95) [41]. There are no data to support the use of bone scan in surveillance of SCLC.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
B. CT abdomen and pelvis with IV contrast

The predominant failure pattern for stage III SCLC is distant metastases, and the most frequent metastatic sites for SCLC in the abdomen are the liver, adrenal glands, and bones. Up to 60% of patients with SCLC have metastases to the abdominal organs at presentation. The liver and adrenal gland are the most frequent site of hematogenous metastasis. Traditionally, CT abdomen with IV contrast has been used to evaluate for extrathoracic metastases and distinguish between LS-SCLC and ES-SCLC. CT abdomen and pelvis after IV contrast administration increases the sensitivity for detection of solid organ metastases. Per the most current ASCO guidelines, CT of the chest with IV contrast and including the adrenal glands is recommended every 2 to 6 months (more frequently in years 1 to 2 and less frequently thereafter), although per the NCCN guidelines, subsequent surveillance imaging usually involves CT of the chest, abdomen, and pelvis (not mentioned if with IV contrast) every 2 to 3 months during year 1, followed by every 3 to 4 months in year 2, biannually in year 3, and then annually [42]. However, per the ASCO guidelines, in patients with no suspected recurrence posttreatment of SCLC, there is no evidence of an added benefit for a CT of the abdomen and pelvis over a CT of the chest including the adrenals [5]. Therefore CT abdomen and pelvis with IV contrast is unlikely to be recommended and used as a standalone procedure without chest CT.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
C. CT abdomen and pelvis without and with IV contrast

The predominant failure pattern for stage III SCLC is distant metastases, and the most frequent metastatic sites for lung cancer in the abdomen are the liver, adrenal glands, and bones. No prior

high-quality studies or randomized trials evaluate the role of body imaging for surveillance after SCLC treatment. Although having pre- and postcontrast imaging can help for better characterization of lesions, especially in the abdomen, there are no recommendations to image the patients both before and after IV contrast administration. Per the ASCO guidelines, in patient with no suspected recurrence posttreatment of SCLC, there is no evidence of an added benefit for a CT of the abdomen and pelvis over a CT of the chest including the adrenals [5].

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
D. CT abdomen and pelvis without IV contrast

The predominant failure pattern for stage III SCLC is distant metastases, and the most frequent metastatic sites for lung cancer in the abdomen are the liver, adrenal glands, and bones. Absence of IV contrast limits the evaluation of solid organs such as the liver, lowering the sensitivity of the examination. Also, per the ASCO guidelines, in patient with no suspected recurrence posttreatment of SCLC, there is no evidence of an added benefit for a CT of the abdomen and pelvis over a CT of the chest including the adrenals, and it would be unlikely to be ordered as a standalone procedure without chest CT [5].

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
E. CT chest abdomen pelvis with IV contrast

SCLC are high-grade neuroendocrine tumors with a high sensitivity to initial therapy and a tendency to recur/progress due to developed chemoresistance [43]. There are 2 main advantages from follow-up: early detection of asymptomatic recurrences and second primaries.

There is disparity with regards to optimal surveillance modalities after completion of follow-up imaging. Per ASCO guidelines, patients with curatively treated stage I-III SCLC with no clinical suspicion of recurrent disease, a diagnostic chest CT including the adrenal glands with IV contrast (preferred) is recommended when conducting surveillance for recurrence during the first 2 years posttreatment, however, per the NCCN guidelines, subsequent surveillance imaging usually involves CT of the chest, abdomen, and pelvis (not mentioned if with IV contrast) every 2 to 3 months during year 1, followed by every 3 to 4 months in year 2, biannually in year 3, and then annually [43-45].

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
F. CT chest abdomen pelvis without and with IV contrast

There is no literature to support and recommend CT imaging of chest, abdomen, and pelvis without and with IV contrast. Per the ASCO guidelines, in patient with no suspected recurrence posttreatment of SCLC, there is no evidence of an added benefit for a CT of the abdomen and pelvis over a CT of the chest including the adrenals [5].

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
G. CT chest abdomen pelvis without IV contrast

It is preferrable for the CT chest, abdomen, and pelvis to be with IV contrast, but it can be performed without IV contrast. Absence of IV contrast limits evaluation of the hilar lymph nodes and mediastinal structures in the chest, as well as solid organs such as the liver in the abdomen,

lowering the sensitivity of the examination for detecting locoregional recurrences and distant metastasis [42].

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
H. CT chest with IV contrast

Of the patients with treated SCLC with limited-stage I-III, 40% will relapse after the first year of treatment, and this increases to 60% after the third year [42].

A large percentage of SCLCs are central in location, arising from the lobar or main bronchi with frequent mediastinal and hilar involvement as well as encasement of vessels, airways, and the esophagus. These are usually treated with chemoradiation, and initial imaging follow-up after completion of therapy includes CT of the chest, abdomen, and pelvis and MRI of the brain. 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, differentiation of central obstructing tumor from surrounding atelectasis, and assessment for liver metastases [46].

As mentioned before, there is disparity with regards to optimal surveillance modalities after completion of follow-up imaging. Per ASCO guidelines, patients with curatively treated stage I-III SCLC with no clinical suspicion of recurrent disease, a diagnostic chest CT including the adrenal glands with IV contrast (preferred) is recommended when conducting surveillance for recurrence during the first 2 years posttreatment. Per the NCCN guidelines, subsequent surveillance imaging usually involves CT of the chest, abdomen, and pelvis every 2 to 3 months (not mentioned if with IV contrast) during year 1, followed by every 3 to 4 months in year 2, biannually in year 3, and then annually [44,45].

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
I. CT chest without and with IV contrast

CT of the chest is the optimal imaging modality for lung cancer surveillance, however, there is no data to support the benefit of CT chest without and with IV contrast over CT chest with IV contrast.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
J. CT chest without IV contrast

Although contrast-enhanced CT detects enlarged hilar lymph nodes with greater accuracy and less interreader variability compared with nonenhanced CT, detection of mediastinal lymph nodes is not typically affected.
NCCN guidelines recommend low-dose CT as the imaging modality of choice for early postoperative follow-up in patients with lung cancer treated with curative intent and with no signs of clinical or radiographic disease [39].

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
K. CT head with IV contrast

CT head with IV contrast can be used as an alternate imaging modality in patients with SCLC. Although MRI has a greater sensitivity for small brain metastases, CT scanning of the brain is an

appropriate method of evaluating for brain metastases in patients with SCLC.

The predominant failure pattern for stage III lung cancer is distant metastases. The incidence of brain metastases is higher in SCLC than in NSCLC. The cumulative incidence is >50% among patients with limited-stage disease and 60% among patients with extensive disease. It is important to detect brain metastases to treat them early before any potential debilitating neurologic symptoms. The NCCN guideline recommends brain MRI (preferred) or brain CT with IV contrast regardless of the prophylactic brain irradiation status [42].

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
L. CT head without and with IV contrast

There is no relevant literature supporting the use of CT head without and with IV contrast for treated lung cancer surveillance.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
M. CT head without IV contrast

The predominant failure pattern for stage III lung cancer is distant metastases. The NCCN SCLC guidelines recommends brain MRI (preferred) or brain CT with IV contrast for all patients with treated SCLC on surveillance, regardless of the PCI status [42].

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
N. CT neck with IV contrast

Although CT neck with IV contrast may be useful for detection of metastatic lymphadenopathy, there is no relevant literature supporting its isolated use for treated lung cancer surveillance.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
O. CT neck without and with IV contrast

There is no relevant literature supporting the use of CT neck without and with IV contrast for treated lung cancer surveillance.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
P. CT neck without IV contrast

There is no relevant literature supporting the use of CT neck without IV contrast for treated lung cancer surveillance.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
Q. CTA chest with IV contrast

Pulmonary thromboembolism is common in patients with lung cancer, and incidence is increased by surgery, chemotherapy, radiotherapy, and disease progression. Although CTA of the chest with IV contrast can frequently detect recurrence, it is typically reserved for patients with symptoms suggestive of pulmonary embolism and is not commonly used for routine surveillance.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.

R. CTA chest without and with IV contrast

There is no relevant literature to support the use of CTA chest without and with IV contrast for routine surveillance imaging of patients with lung cancer treated with curative intent.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
S. FDG-PET/CT skull base to mid-thigh

Evidence of the potential usefulness of FDG-PET/CT in surveillance of SCLC is scarce, and its utility for routine follow-up and surveillance of SCLC is indeterminate but may be appropriate.

NCCN guidelines recommend FDG-PET/CT in the staging of SCLC or combined SCLC/NSCLC only if limited-stage disease is suspected, along with brain MRI or contrast-enhanced CT. In patients with established ES-SCLC, further staging with FDG-PET/CT is optional. 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 patients with SCLC [47-49]. FDG-PET scan has a superior sensitivity and specificity compared with CT in the identification of metastatic disease other than brain metastases in patients with SCLC.

Despite FDG-PET/CT value in the early detection of recurrence, which could affect management decisions during the follow-up period, the effectiveness in this context has not been systematically established in clinical practice, and there are no clinical practice guideline recommendations for the routine use of FDG-PET/CT in assessing posttreatment follow-up for patients with SCLC [39]. FDG-PET/CT may be useful in 2 scenarios: further characterization of abnormal CT findings or detection of recurrence within/around an area of radiation change because, in some cases, delineation of viable tumor is difficult on standard morphologic imaging such as CT or MR. The added value of FDG-PET/CT in individualizing patient management depends on the prior clinical or imaging suspicion of disease [50].

Imaging Following RFA: A pattern of focally intense and increasing FDG-PET uptake has a high sensitivity and specificity for detecting recurrent lung cancer following RFA. Surveillance after RFA should include a contrast-enhanced diagnostic CT at 1 month to diagnose procedural complications, PET at 6 months as a posttreatment metabolic baseline (with diagnostic CT if PET is abnormal), and alternating diagnostic CTs or PET every 6 months for 2 years [30]. PET/CT after RFA has a high rate of false-positives in the immediate post-RFA phase (30 days) and initial 6 month period, when it can show prominent nonfocal increased uptake in the ablation zone, however, this regresses in the 6-to 12-month period. In this setting, dual-energy CT shows promise in detecting early recurrence post-RFA. In a study by Izaaryene et al [31], the sensitivity of dual-energy CT for detecting lung cancer recurrence at 1 month follow-up after RFA was 100%, with a specificity of 85.71% and an NPV of 100%.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
T. MRI chest without and with IV contrast

Although MRI chest may have a value in the staging of lung cancer, there is no relevant literature supporting its benefit in lung cancer surveillance.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-

III small-cell lung cancer. Routine surveillance.
U. MRI chest without IV contrast

Although MRI chest may have a value in the staging of lung cancer, there is no relevant literature supporting its benefit in lung cancer surveillance. DWI can potentially differentiate benign from malignant nodes, which have increased cellularity and less extracellular space [32,33]. Therefore, the diffusion of water in malignant lesions is restricted, resulting in a decreased apparent diffusion coefficient [32,34]. This technique showed lower false-positive findings for NSCLC staging compared with FDG-PET/CT and was highly accurate in distinguishing lymphadenitis from malignant nodes. Further studies are needed to test DWI accuracy for the detection of lung cancer recurrence after surgery, particularly when FDG-PET/CT findings are equivocal.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
V. MRI head without and with IV contrast

The incidence of brain metastases is higher in SCLC than in NSCLC. The cumulative incidence is >50% among patients with limited-stage disease and 60% among patients with extensive disease. Therefore, MRI head with IV contrast is recommended in all patients with SCLC. Per the ASCO guidelines, for patients who have undergone curative-intent treatment for stage I-III SCLC and did not receive PCI, clinicians should offer brain MRI every 3 months for the first year and every 6 months for the second year for surveillance. The same schedule may be offered for patients who did receive PCI, however, brain MRI should not be routinely offered to asymptomatic patients after 2 years of disease-free survival [5]. MRI head identifies metastatic lesions in 10% to 15% of patients with newly diagnosed SCLC without neurologic symptoms [51]. MRI is more sensitive than CT for the detection of intracranial metastases. If there is history of contrast allergy, MRI head without IV contrast may be performed.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
W. MRI head without IV contrast

Although brain MRI is more sensitive for detecting metastatic disease than brain CT, contrast increases the specificity for detection of metastatic disease especially in the case of leptomeningeal spread.

Variant 2: Variant 2: Adult. Noninvasive imaging surveillance following treatment of stage I-III small-cell lung cancer. Routine surveillance.
X. Radiography chest

Approximately 80% of patients with LS-SCLC and almost all patients with extensive-stage disease relapse, most commonly in the first year after treatment [52]. Two decades ago, the ACCP recommended surveillance for patients with lung cancer treated with curative intent using chest radiograph or CT [53], however, CT imaging was proven more sensitive than conventional chest radiography for detecting tumor recurrence [5], and hence radiography has no current role in surveillance.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.

Recurrent NSCLC may manifest as locoregional or distant disease. Recurrence in the same hemithorax as the primary tumor is considered locoregional recurrence and includes disease in the treated tumor bed, bronchial stump, ipsilateral nodes, pleura, and chest wall, although some

include contralateral mediastinal and supraclavicular nodes. Locoregional recurrence has been reported in 34% to 50% of patients, and distant recurrence has been reported in50% to 66% of patients. Common sites of distant metastases include brain, bone, liver, adrenal glands, and distant nodes. Patients with stage IIIA disease have a higher rate of symptomatic presentation, higher risk of recurrence, and propensity for distant recurrence than patients with stage I or II disease [54,55]. Patients with local recurrence after having undergone surgery or radiation therapy may be candidates for additional resection or radiation therapy if there are no distant metastases.

Conforti et al [9] undertook a multivariate analysis to identify variables associated with increased risk of recurrence, finding increased risk associated with positive lymph node status (HR 2.00; 95% CI, 1.54-2.61) and limited/minimal mediastinal lymph node sampling as compared with systematic mediastinal lymph node dissection (HR 1.43; 95% CI, 1.10-1.86). Factors associated with increased risk of distant metastatic recurrence included T3/4 pathologic stage (HR 1.30; 95% CI, 1.01-1.68) and positive lymph node status (HR 1.76; 95% CI, 1.4-2.18), whereas there was some protective effect in never smokers (HR 0.64; 95% CI, 0.47-0.88) and nonsquamous tumors (HR 0.40; 95% CI, 0.33-0.49).

Stirling et al [7] did a systematic review and meta-analysis of follow-up surveillance after curative-intent treatment of NSCLC and found that the recurrence rates varied between 17.8% and 71%. Rates of recurrence were lower, 11.1% to 22%, in earlier stage (stage I-II) disease and higher, 52% to 72% in those with higher-stage disease (stage IIIA) [7,56,57].

Scheduled imaging detected recurrence/SPLC in 60% to 100% of cases, and symptomatic presentation led to detection by unscheduled imaging in 0% to 40% of cases [9,58]. Lou et al [56] observed a higher detection rate of asymptomatic recurrences among patients with early stage by surveillance CT scans, with 32% of detected recurrences in the early-stage cohort (stage I-II) identified as a result of symptoms during unscheduled follow-up compared with 61% among patients in stage IIIA (I = .04).

In usual clinical practice, a patient with clinical or radiographic suspicion of NSCLC recurrence is fully restaged with IV contrast chest CT, PET/CT, and brain MRI.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
A. Bone scan whole body

Lung cancer is the third most common form of cancer to spread to bones. Approximately 30% to 40% of patients with lung cancer develop bone metastases during the course of their disease. Pain is usually the first symptom of osseous metastases in 80% of patients [59]. A meta-analysis comparing the capability of FDG-PET, FDG-PET/CT, MRI, and bone scintigraphy to detect bone metastases in patients with lung cancer showed that both FDG-PET/CT and FDG-PET were superior to MRI and bone scintigraphy. FDG-PET/CT has higher diagnostic value (sensitivity, specificity) than any other imaging modalities [41], because of its ability to detect the presence of tumors directly by metabolic activity rather than indirectly by increased bone mineral turnover.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
B. CT abdomen and pelvis with IV contrast

CT abdomen and pelvis with oral and IV contrast is suggested in patients with NSCLC with

abnormal clinical evaluation, including signs and symptoms referable to the abdomen and pelvis and no suspicious extrathoracic findings on chest CT. In addition, all patients with NSCLC with locally advanced stage III or stage IV disease should undergo extrathoracic imaging with CT abdomen and pelvis or FDG-PET/CT because of a high incidence of occult extrathoracic metastatic disease in up to 37% patients.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
C. CT abdomen and pelvis without and with IV contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast for the evaluation of suspected recurrence in patients with curatively treated NSCLC.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
D. CT abdomen and pelvis without IV contrast

Iodinated contrast enhancement is vital to the detection of solid organ metastases on CT. There is no relevant literature to support the use of noncontrast CT abdomen and pelvis for the evaluation of suspected recurrence in patients with curatively treated NSCLC.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
E. CT chest abdomen pelvis with IV contrast

Patients with a history of treated NSCLC and new onset weight loss; deep-seated pain in the chest, back, and arms; and abdominal pain and swelling should undergo evaluation with CT chest, abdomen, and pelvis with IV contrast [20].

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
F. CT chest abdomen pelvis without and with IV contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast for the evaluation of suspected recurrence in patients with lung cancer treated with curative intent.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
G. CT chest abdomen pelvis without IV contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without IV contrast for the evaluation of suspected recurrence in patients with lung cancer treated with curative intent. 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, differentiation of central obstructing tumor from surrounding atelectasis, and assessment for liver metastases [46].

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
H. CT chest with IV contrast

For patients with suspected recurrence within the lungs (new cough, wheezing, chest pain, shortness of breath, or hemoptysis), chest CT including the upper abdomen with IV contrast is preferred. Recurrent NSCLC may manifest as locoregional or distant disease. Locoregional

recurrence has been reported in 34% to 50% of patients and distant recurrence in 50% to 66% of patients.

Conforti et al [9] reported on 2,261 patients observing a significantly higher likelihood of detection of locoregional recurrences by scheduled follow-up compared with unscheduled detection (88.4%; 95% CI, 84%-91%) and SPLC (93.2%; 95% CI, 84%-99%), but not for distant metastases (68.7%; 95% CI, 65%-73%, P < .0001). Hence, there is good evidence for performing chest CT for early detection of locoregional recurrence. Patients with local recurrence after having undergone surgery or radiation therapy may be candidates for additional resection or radiation therapy in the absence of distant metastatic disease.

New or enlarging lymph nodes with a short axis ≥1 cm on CT are considered suspicious for disease recurrence and must be investigated further by FDG-PET/CT and/or transbronchial biopsy. The sensitivity and specificity of CT for the detection of mediastinal lymph node metastasis are reported as 50% to 70% and 65% to 85%, respectively, whereas the corresponding values for PET/CT are 75% to 85% and 85% to 90%, respectively. Transbronchial needle aspiration is more sensitive than CT. For example, in a study of 10 patients with biopsy-proven metastatic lymphadenopathy precluding surgery, in half of them, the final nodal stage was diagnosed at CT; the other half had biopsy-proven metastatic lymph nodes not enlarged by CT criteria [60,61]. In another study by Al-Ibraheem et al [62], the NPVs of mediastinoscopy, endobronchial ultrasound/transbronchial needle aspirate (EBUS/TBNA), and FDG-PET/CT were 87.1%, 90.91%, and 83.33%, respectively. The overall accuracy was highest for mediastinoscopy (88.6%) and EBUS/TBNA (88.2%), followed by FDG-PET/CT (70.2%). The NPV of FDG-PET/CT was considered reliable and comparable to the NPV of EBUS/TBNA. The authors concluded that SUVmax of lymph nodes could help in predicting metastases, but nevertheless, a positive FDG-PET/CT should be verified histopathologically particularly if such a result would change the treatment plan.

Pleural recurrence can manifest as pleural nodules or pleural effusions and has been reported in 6% to 16.8% of patients who undergo surgery [63].

In 2 different studies done by Hanna et al [37] and Gambazzi et al [8], the sensitivity for the detection of recurrent disease was 21.2% by chest radiography, 93% to 94.2% by CT, and 80.8% to 94.4% by PET/CT. Specificity for detection of recurrent disease was 91.7% by chest radiography, 72.0% to 86.0% by CT, and 62.0% to 97.6% by PET/CT [8,37].

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
I. CT chest without and with IV contrast

There is no relevant literature to support the use of CT chest without and with IV contrast for the evaluation of suspected recurrence in patients with lung cancer treated with curative intent.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
J. CT chest without IV contrast

Noncontrast chest CT is adequate for the identification of new lung nodules. It also identifies pleural or pericardial effusions that may need cytological confirmation as sites of disease if pleural or pericardial nodules are not visible. Differentiating recurrence on noncontrast CT scans from postsurgical changes (such as atelectasis or muscle flap) may be challenging. A soft tissue nodule

near the surgical clips may represent either granulation tissue or tumor recurrence. On follow-up with serial CT scans, the interval growth of solid or subsolid nodule close to the staple line is suggestive of recurrence [20].

Osseous metastases and extra thoracic metastases involving the adrenal glands may also be seen on a noncontrast chest CT, however, adrenal nodules may not be definitively characterized by CT if intracytoplasmic lipid content is low, which occurs in approximately one-third of adrenal adenomas [19].

In patients with stage III unresectable disease who have undergone chemoradiation, use of contrast-enhanced CT is preferred over unenhanced CT, because the former offers greater accuracy and reduced interreader variability in the identification of hilar lymph nodes, as well as reliable detection of mediastinal lymph nodes and abdominal progression [18].

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
K. CT head with IV contrast

Although brain imaging with CT or MRI is not useful as a routine surveillance tool in asymptomatic patients with curatively treated NSCLC, CT head with IV contrast can be used as an alternative imaging modality in patients with stage III or IV NSCLC or those with neurological symptoms. Although MRI has a greater sensitivity than CT, identification of a greater number and smaller brain lesions on MRI compared with CT has not been associated with better survival [64].

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
L. CT head without and with IV contrast

There is no relevant literature to support the use of CT head without and with IV contrast for the evaluation of suspected recurrence in patients with NSCLC.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
M. CT head without IV contrast

There is no relevant literature to support the use of CT head without IV contrast for the evaluation of suspected recurrence in patients with NSCLC. Noncontrast head CT alone is not sensitive enough to screen for cerebral metastases, but findings can suggest the diagnosis of underlying metastases. In the absence of hemorrhage, metastases may be hypodense, isodense, or hyperdense compared with the brain. Acutely hemorrhagic metastases appear hyperdense to brain.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
N. CT neck with IV contrast

There is no relevant literature to support the use of CT neck with IV contrast in patients with curatively treated NSCLC, however, CT neck may be performed if the patient has new neck mass or suspected adenopathy. In patients with suspected supraclavicular nodes on physical examination, contrast CT of the chest from the level of the thoracic inlet may confirm or exclude presence of enlarged supraclavicular nodes. In patients with new onset hoarseness, CT scan of the neck and chest (and in some cases brain MRI) may help to exclude mass along the course of the recurrent

laryngeal nerve.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
O. CT neck without and with IV contrast

There is no relevant literature to support the use of CT neck without and with IV contrast for the evaluation of suspected recurrence in patients with lung cancer treated with curative intent.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
P. CT neck without IV contrast

There is no relevant literature to support the use of CT neck without IV contrast for the evaluation of suspected recurrence in patients with lung cancer treated with curative intent.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
Q. CTA chest with IV contrast

Pulmonary thromboembolism is common in patients with lung cancer, and incidence is increased by surgery, chemotherapy, radiotherapy, and disease progression. CTA evaluation may be useful in patients with NSCLC with new onset hemoptysis, chest pain, or worsening dyspnea, which may be caused by tumor recurrence/disease progression or due to pulmonary embolism.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
R. CTA chest without and with IV contrast

There is no relevant literature to support the use of CTA chest without and with IV contrast for evaluation of suspected recurrence in imaging of patients with lung cancer treated with curative intent.

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
S. FDG-PET/CT skull base to mid-thigh

NSCLC is characterized by a high incidence of extrathoracic recurrence. Common sites of distant metastases include brain, bone, liver, adrenal glands, and distant nodes. Patients with stage III disease have a higher rate of symptomatic presentation, higher risk of recurrence, and propensity for distant recurrence than patients with stage I or II disease [54,55]. Although no current guidelines favor PET/CT over CT, the enhanced ability of PET/CT to detect extrathoracic recurrence addresses the third postulate of Edelman et al (ie, tests should be directed at the most likely sites of recurrence with high positive and NPVs, that is, test accuracy) [65]. Per the current NCCN guidelines, PET/CT and brain MRI are preferred after chest CT provides suspicion of relapse [6,42].

Few studies showed the sensitivity and specificity of PET/CT to detect recurrent disease to be in the range of 80.8% to 94.4% and 62.0% to 97.6%, respectively [8,23,58].

Choi et al [21] reported on 111 disease recurrences among 358 patients and observed locoregional recurrence in 29 of 111 (26.1%) who had significantly longer median survival than those with distant metastases (mean ± SE, 4.2 ± 0.3 y versus 3.0 ± 0.2 y; P = .008). Patients with disease recurrence detected by CT had superior survival to those detected by history and physical examination, and patients with disease recurrence detected by PET/CT and CT had a nonsignificant

trend to longer survival than CT detected recurrence alone (mean ± SE, 3.8 ± 0.2 y versus 3.3 ± 0.3 y; P = .179).

A meta-analysis comparing the capability of FDG-PET, FDG-PET/CT, MRI, and bone scintigraphy to detect bone metastases in patients with lung cancer showed that both FDG-PET/CT and FDG-PET were superior to MRI and bone scintigraphy. FDG-PET/CT has a higher diagnostic value (sensitivity, specificity) than any other imaging modalities [41], likely due to its ability to detect the presence of tumors directly by metabolic activity rather than indirectly by increased bone mineral turnover. The sensitivity, specificity, accuracy, and NPV of FDG-PET for bone metastases is >90% and is superior to bone scintigraphy. The study by Onishi et al [58] also suggests that PET/CT provides a diagnostic accuracy similar to that of multimodality imaging encompassing brain MRI using contrast, contrast-enhanced whole body CT, and bone scintigraphy.

The liver and adrenal gland are the most frequent site of hematogenous metastasis. 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%. When findings are discordant or indeterminate, MRI or biopsy is an appropriate strategy to evaluate liver lesions. FDG-PET has a sensitivity of 94% and specificity of 82% for the 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. Patients with an FDG-avid adrenal nodule as the only site of potential metastatic disease require biopsy confirmation [66].

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
T. MRI chest without and with IV contrast

MRI chest without and with IV contrast may be indicated in specific clinical circumstances in patients with NSCLC with suspected recurrence and equivocal findings on CT chest. Focused MRI of the chest may be useful in the assessment of chest wall or spinal invasion and tumor involvement of mediastinal structures including the heart, great vessels, or pericardium. MRI is superior to CT for detecting involvement of the brachial plexus, neural foramina, and spinal canal. MRI is also capable of distinguishing an obstructing tumor from post–obstructive 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 [67].

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer. Suspected recurrence or progression.
U. MRI chest without IV contrast

There is no relevant literature to support the use of MRI chest without IV contrast for the evaluation of suspected recurrence in patients with lung cancer treated with curative intent. DWI can potentially differentiate benign from malignant nodes, which have increased cellularity and less extracellular space [32,33]. Therefore, the diffusion of water in malignant lesions is restricted, resulting in a decreased apparent diffusion coefficient [32,34]. This technique showed lower false-positive findings for NSCLC staging compared with FDG-PET/CT and was highly accurate in distinguishing lymphadenitis from malignant nodes. In a study by Usuda et al [68], there was restricted diffusion in each case of recurrence (NSCLC, carcinoid). The detection rate for recurrence was 100% in DWI, 98% in PET/CT, and 82% in CT, and hence, the detection rate of DWI was significantly higher than that of CT (P = .0244) but nearly similar to that of PET/CT (P = .22).

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer.

Suspected recurrence or progression.
V. MRI head without and with IV contrast

MRI head without and with IV contrast is useful in all patients with NSCLC with neurologic symptoms, regardless of stage. MRI head is the preferred imaging modality for the evaluation of intracranial metastases, because it is more sensitive for small brain lesions than CT [64]. In the current NCCN guidelines, PET/CT and brain MRI are preferred after chest CT provides suspicion of relapse [6].

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer.
Suspected recurrence or progression.
W. MRI head without IV contrast

Brain MRI is more sensitive for detecting metastatic disease than head CT, with studies showing an additive value of MRI in the detection of additional unsuspected brain and meningeal metastases in up to 4.7% patients without suspect lesions on contrast-enhanced CT. Furthermore, the use of contrast increases the sensitivity and specificity for the detection of smaller parenchymal lesions as well as metastatic disease involving the leptomeninges [69].

Variant 3: Adult. Posttreatment evaluation of stage I-III non–small-cell lung cancer.
Suspected recurrence or progression.
X. Radiography chest

Although chest radiograph is not sensitive or specific for detecting disease recurrence, it is often used as an initial test in patients with suspected lung cancer recurrence to detect acute findings such as pneumothorax, which may be a complication of treatment or else may follow thoracentesis, and also to detect pneumonia or drug-induced pneumonitis as an explanation for the patient's symptoms. In a study by Hanna et al [37], the sensitivity for detection of recurrent disease by chest radiography was low at 21.2%, whereas the specificity was 91.7%, although the sensitivity and specificity by CT were approximately 93% to 94.2% and 72% to 86%, respectively [8,37].

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer.
Suspected recurrence or progression.

SCLC is typically very responsive to chemotherapy, and the rates of response to first-line combination chemotherapy are 60% to 70% (53) [70]. Despite high response rates to first-line combination chemotherapy, approximately 80% of patients with LS-SCLC and virtually all patients with ES-SCLC develop recurrent or progressive disease. On the basis of Surveillance, Epidemiology, and End Results data in the United States, the 5- year survival rates are approximately 10% to 15% for patients with LS-SCLC and 1% to 2% for patients with ESSCLC. Patients with LS-SCLC have a median survival time of 15 to 20 months, whereas those with ES-SCLC have a median survival time of 8 to 10 months and a 2-year survival rate of 10% [71,72]. LS-SCLC usually manifests in a stage III pattern; stage I or II disease is rarely encountered clinically. Also, the disease stage in patients with SCLC correlates with development of distant metastasis and brain metastasis, however, local failure rates or local progression does not correlate well with disease stage and is a relatively infrequent mode of failure [73].

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer.
Suspected recurrence or progression.
A. Bone scan whole body

Overall, the most common sites of metastases are bone (19%-38%), liver (17%-34%), adrenal

glands (10%-17%), and brain (up to 14%) [40]. FDG-PET/CT is typically performed in patients with SCLC, however, if FDG-PET/CT is unavailable, bone scintigraphy with Tc-99m methylene diphosphonate and CT of the chest abdomen pelvis with IV contrast are preferred.

In a meta-analysis study performed by Qu et al [41], it was found that bone scintigraphy was unable to detect osseous metastasis at an early stage. Bone scintigraphy was also unable to differentiate trauma, healing fractures, benign neoplasm, and degenerative disease from metastasis. The sensitivity of bone scan for lung cancer metastasis detection was 86% (95% CI, 0.82-0.89) versus 92% for FDG-PET/CT (95% CI, 0.88-0.95) [41].

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
B. CT abdomen and pelvis with IV contrast

The predominant failure pattern for SCLC is distant metastases, and the most frequent sites for metastases are the liver, adrenal glands, and bones. Therefore, patients with a history of treated SCLC and new onset weight loss, abdominal pain, and swelling should undergo evaluation with CT abdomen and pelvis after IV contrast administration to increase the sensitivity for detection of solid organ metastases. For the current NCCN update, the algorithm now states that if there is clinical or radiographic suspicion for recurrence, a restaging CT chest with IV contrast (plus/minus abdomen/pelvis), FDG-PET/CT, and brain MRI should be done [6,42,43].

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
C. CT abdomen and pelvis without and with IV contrast

The predominant failure pattern for SCLC is distant metastases, and the most frequent sites for metastases are the liver, adrenal glands, and bones. Therefore, enhanced CT abdomen and pelvis after IV contrast administration may be done to increase the sensitivity for detection of solid organs metastases. For the current NCCN update, the algorithm now states that if there is clinical or radiographic suspicion for recurrence, a restaging chest CT with IV contrast (plus/minus abdomen/pelvis), FDG-PET/CT, and brain MRI should be done [42,43]. There is no literature to support the use of CT abdomen and pelvis before and after IV contrast.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
D. CT abdomen and pelvis without IV contrast

Although it is preferrable to perform CT abdomen and pelvis with IV iodinated contrast, it can be performed without IV contrast and can detect large solid visceral lesions and adenopathy as well as ascites. Absence of IV contrast limits the evaluation of smaller metastases within solid organs such as the liver and spleen, lowering the sensitivity of the examination, thus making it less useful than an examination with IV contrast.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
E. CT chest abdomen pelvis with IV contrast

SCLC are high-grade neuroendocrine tumors with a high sensitivity to initial therapy and a tendency to recur/progress due to developed chemoresistance [43]. Patients with a history of treated SCLC and new onset weight loss; deep-seated pain in the chest, back, and arms; and abdominal pain and swelling should undergo evaluation with CT chest, abdomen, and pelvis with

IV contrast. Most patients with SCLC manifest with ES-SCLC III or IV disease with development of distant metastases. It has been shown that the development of distant metastasis (liver, adrenals, bones, and brain) correlates with disease stage in patients with SCLC, whereas local progression (lung, regional lymph nodes) does not correlate well with stage and is a relatively infrequent mode of failure. Therefore, in patients with suspected recurrence, PET/CT and/or enhanced CT of the chest, abdomen, and pelvis combined with MRI head is useful to evaluate for recurrences [73].

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
F. CT chest abdomen pelvis without and with IV contrast

Although having pre- and postcontrast imaging can help for better characterization of lesions especially in the abdomen, there are no recommendations to image the patients both before and after IV contrast.
CT Chest Abdomen Pelvis Without IV Contrast

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
G. CT chest abdomen pelvis without IV contrast

It is preferrable for the CT chest, abdomen, and pelvis to be with IV contrast, but it can be performed without IV contrast. Absence of IV contrast limits evaluation of the hilar lymph nodes and mediastinal structures in the chest, as well as solid organs such as the liver in the abdomen, lowering the sensitivity of the examination.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
H. CT chest with IV contrast

Of the patients with treated SCLC with LS-SCLC I-III, 40% will relapse after the first year of treatment, and this increases to 60% after the third year [42]. Progression is usually aggressive. Diagnostic CT chest, preferably with IV contrast and including the adrenals, should be performed if the patient has new onset cough, hemoptysis, wheezing, or chest pain [5]. Chest CT with IV contrast can aid in the identification of chest wall invasion, assess for mediastinal and vascular invasion, evaluate for recurrence in mediastinal and hilar lymph nodes, differentiate tumor from surrounding atelectasis, and evaluate radiation change, and is also useful for evaluation of liver or adrenal metastases.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
I. CT chest without and with IV contrast

CT of the chest is the optimal imaging modality for the detection of lung cancer recurrence, however, there are no data to support the benefit of CT chest without and with IV contrast over CT chest with IV contrast.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
J. CT chest without IV contrast

Although contrast-enhanced CT detects enlarged hilar lymph nodes with greater accuracy and less interreader variability compared with nonenhanced CT, detection of mediastinal lymph nodes is not typically affected and could be performed in certain situations [5].

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer.

Suspected recurrence or progression.
K. CT head with IV contrast

The predominant failure pattern for SCLC is distant metastases. The incidence of brain metastases is higher in SCLC than in NSCLC. The cumulative incidence is >50% among patients with limited-stage disease and 60% among patients with extensive disease. It is important to detect brain metastases to treat them early before any potential debilitating neurologic symptoms. The NCCN SCLC guidelines recommend brain MRI (preferred) or CT head with IV contrast regardless of the prophylactic brain irradiation status [42]. Brain MRI with IV contrast is preferred in patients who do not receive PCI based on the ASCO guideline [43].

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
L. CT head without and with IV contrast

There is no relevant literature supporting the use of CT head without and with IV contrast for suspected SCLC recurrence.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
M. CT head without IV contrast

The predominant failure pattern for SCLC is distant metastases. Although CT head without IV contrast can be more sensitive for the detection of intracranial bleed or calcifications than a CT with IV contrast, the NCCN SCLC guidelines recommends brain MRI (preferred) or brain CT with IV contrast for all patients with treated SCLC on surveillance, regardless of the PCI status [42]. However, if the patient presents with acute complaint, nonenhanced CT of the head may be done to rule out bleeding.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
N. CT neck with IV contrast

CT neck with IV contrast may be helpful if there are localized neck findings such as lymphadenopathy that are suspicious for disease recurrence.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
O. CT neck without and with IV contrast

There is no relevant literature supporting the use of CT neck without and with IV contrast in a patient with suspected disease recurrence.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
P. CT neck without IV contrast

There is no relevant literature supporting the use of CT neck without IV contrast in a patient with suspected disease recurrence.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
Q. CTA chest with IV contrast

Pulmonary thromboembolism is common in patients with lung cancer, and incidence is increased by surgery, chemotherapy, radiotherapy, and disease progression. CTA evaluation may be useful in

patients with new onset hemoptysis or chest pain, which may be caused by tumor recurrence/disease progression or from pulmonary embolism.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
R. CTA chest without and with IV contrast

There is no relevant literature to support the use of CTA chest without and with IV contrast for imaging of patients with suspected lung cancer recurrence.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
S. FDG-PET/CT skull base to mid-thigh

FDG-PET/CT is frequently used in cases of suspected recurrent disease especially involving patients who are candidates for salvage treatment. SCLC is readily identified on FDG-PET/CT because of its high metabolic activity and because it is more sensitive and specific than conventional imaging for detecting metastatic disease [74]. Combined FDG-PET/CT helps in identifying recurrent disease earlier, which leads to timely management. Recent studies have supported the use of FDG-PET/CT for the detection of recurrent lung cancer. The pooled sensitivity and specificity were found to be 90% and 90%, respectively, for FDG-PET/CT and 78% and 80%, respectively, for conventional imaging techniques (eg, radiography, CT, bone scintigraphy, and MRI) [75,76]. Furthermore, FDG-PET/CT may be useful in assessing focal lesions on chest CT, which may be due to radiation fibrosis, atelectasis, or other benign conditions per NCCN, although histopathologic confirmation of FDG-avid lesions is recommended [39]. The added value of posttreatment FDG-PET/CT in individualizing patient management depends on the prior clinical or imaging suspicion of disease. Among patients who underwent follow-up FDG-PET/CT for suspected recurrence, FDG-PET/CT was able to rule out recurrence or metastasis in about one-fourth of the scans [50,77].

For SCLC or combined SCLC and NSCLC, the NCCN recommends performing FDG-PET/CT only if limited-stage disease is suspected, along with brain MRI and contrast-enhanced chest CT. When extensive disease is established, further staging with FDG-PET/CT is optional.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
T. MRI chest without and with IV contrast

Thoracic MRI is not routinely used to evaluate SCLC but may be useful in specific scenarios. For instance, MRI is especially useful for the evaluation of suspected mediastinal or vascular invasion. Although it is not yet recommended in the follow-up of treated lung cancer, MRI and specifically DWI can be useful for the detection of recurrence and metastasis.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
U. MRI chest without IV contrast

Although it is not yet recommended in the follow-up of treated lung cancer, MRI and specifically DWI can be useful for detection of recurrence and metastasis. In a study by Usuda et al [68], there was restricted diffusion in each recurrence. The detection rate for recurrence was 100% in DWI, 98% in PET/CT and 82% in CT, and hence, the detection rate of DWI was significantly higher than that of CT (P = .0244) but not significantly higher than that of PET/CT (P = .22).

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer.

Suspected recurrence or progression.
V. MRI head without and with IV contrast

The current treatment guidelines recommend PCI for all patients with LS-SCLC with a response to initial therapy, regardless of TNM stage. This is due, in part, to the assumption that SCLC is essentially a systemic disease, regardless of macroscopic disease burden. Approximately 10% to 14% of patients with SCLC have brain metastases at the time of diagnosis, and 50% to 60% will develop brain metastases during the course of the disease. A trial conducted by the European Organization for Research and Treatment of Cancer Radiation Oncology and Lung Cancer group demonstrated that PCI decreased the incidence of symptomatic brain metastases and prolonged survival in patients with ES-SCLC [51]. On the basis of these results, PCI is now recommended for patients with either LS-SCLC or ES-SCLC who demonstrate a good response to chemotherapy or chemoradiation therapy.

The NCCN SCLC guidelines recommend brain MRI (preferred) or brain CT with IV contrast every 3 to 4 months during year 1 for all patients and then every 6 months during year 2, regardless of the PCI status. Brain MRI is more sensitive than CT for identifying brain metastases and, therefore, is preferred over CT [42]. Gadolinium-enhanced brain MRI is more sensitive than contrast-enhanced CT brain. In patients with possible recurrence and new neurologic symptoms, brain MRI is useful. In a study by Seute et al [78], detection of brain metastases increased from 10% to 24% once MRI was used in the majority of patients instead of CT. Of note, the survival of patients with single brain metastasis is longer than that of patients with multiple brain metastases.

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
W. MRI head without IV contrast

Brain MRI is more sensitive for detecting metastatic disease than head CT, with studies showing an additive value of MRI in the detection of additional unsuspected brain and meningeal metastases in up to 4.7% patients without suspect lesions on contrast-enhanced CT. Furthermore, the use of contrast increases the sensitivity and specificity for the detection of smaller parenchymal lesions as well as metastatic disease involving the leptomeninges [69].

Variant 4: Variant 4: Adult. Posttreatment evaluation of stage I-III small-cell lung cancer. Suspected recurrence or progression.
X. Radiography chest

Although chest radiograph is not sensitive or specific for detecting disease recurrence, it is often used as an initial test in patients with suspected lung cancer recurrence to detect acute findings such as pneumothorax, which may be a complication of treatment or else may follow thoracentesis, and is also used to detect pneumonia or drug-induced pneumonitis in symptomatic patients. Approximately 80% of patients with LS-SCLC and almost all patients with ES-SCLC relapse, most commonly in the first year after treatment [52]. After surgical resection of lung cancer, minimal dose CT is more sensitive and has a higher NPV than chest radiography for the detection of new or recurrent lung cancer (94% versus 21%; $P < .0001$ and 99% versus 96%; $P = .007$, respectively). The majority of detected cancers by CT were asymptomatic, allowing a curative treatment and improving survival [37].

Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete

narrative document for more information.

- **Variant 1:** For routine noninvasive imaging surveillance of treated stage I-III NSCLC, CT chest with IV contrast is usually appropriate in allowing evaluation of local recurrence at the surgical bed, new lung nodules, or enlarged lymph nodes. CT chest without IV contrast may also be appropriate (disagreement), although assessment of hilar lymph nodes is better performed with IV contrast.
- **Variant 2:** For routine noninvasive imaging surveillance following treatment of stage I-III SCLC, MRI of the head without and with IV contrast (preferred) and MRI of the head without IV contrast are usually appropriate given higher incidence of brain metastases in patients with SCLC. CT chest with IV contrast is also usually appropriate because it can detect both locoregional and metastatic disease within the chest and upper abdomen. CT chest, abdomen, and pelvis with IV contrast and FDG-PET/CT skull base to mid-thigh may be appropriate because liver, bones, and adrenal glands are frequent sites of metastatic disease.
- **Variants 3 and 4:** For posttreatment evaluation of suspected recurrence or progression of stage I-III NSCLC and SCLC, MRI head with and without IV contrast, CT chest with IV contrast, and FDG-PET/CT are usually appropriate for the detection of thoracic locoregional recurrences and extrathoracic metastatic disease, respectively. Radiography of the chest may be helpful in the initial assessment of acute findings to identify treatment-related complications or pneumonia in symptomatic patients that may be initially mistaken clinically for recurrence. MRI of the chest with and without IV contrast may help with troubleshooting findings that are equivocal on chest CT, offering superior assessment of the chest wall, mediastinal structures, and for identifying spinal invasion. Imaging of additional anatomic regions, for instance CT chest abdomen pelvis with IV contrast, CT abdomen and pelvis with IV contrast, or CT of the neck with IV contrast may be appropriate and can be done as clinically indicated based on localized or systemic symptoms.

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.

Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that predates the use of the current understanding of language inclusive of diversity in sex, intersex, gender, and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health.

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
O	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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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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