

## NCCN Guidelines Version 1.2025 Lung Cancer Screening

## **Clinical Management Protocols for LDCT Screening**

LDCT lung cancer screening studies using MDCT scanners have decreased lung cancer mortality in subjects at high risk for lung cancer compared with unscreened or chest radiography-screened cohorts, but have applied varying clinical and imaging management algorithms for defining abnormal screens and the follow-up of nodules or other findings concerning for lung cancer. 9,11,221,222,318,327-331 These algorithms are based on the positive relationships among: 1) nodule size and/or nodule consistency and likelihood of malignancy; 2) nodule size and tumor stage; and 3) tumor stage and survival. They also take into account the average growth rate of lung cancer (ie, volume doubling time). 332-339 Most of these algorithms recommend FDG-PET/CT be considered for nodules that are at least 7 to 10 mm, or dynamic contrast-enhanced CT if FDG-PET/CT is not available, because these technologies have been shown to increase specificity for malignancy. 42,258,261,340-344 FDG-PET has low sensitivity for nodules with <8-mm solid component and for small nodules near the diaphragm or heart where there is motion artifact. In the workup of nodules detected with CT in a lung cancer screening population at high risk for lung cancer, most nodules requiring follow-up undergo interval LDCT, with the roles of contrast-enhanced CT and FDG-PET/CT in evolution, and the latter limited to larger nodules. 345,346

Currently, the most accurate protocol for lung cancer detection using LDCT is difficult to determine because of differing patient populations, methodologies, lengths of follow-up, and statistical analyses among lung cancer screening studies. LDCT screening programs (with multiple years of follow-up) report that 65% to 85% of detected lung cancers are stage I.<sup>10,97,214,317,330,344</sup> The NELSON trial, I-ELCAP (International Early Lung Cancer Action Program), and NLST are the largest series examining lung cancer detection using LDCT in individuals with high-risk factors (see *Benefits of Lung Cancer Screening* in this Discussion).<sup>9,10,334,347,348</sup> To help ensure good image quality, all LDCT screening programs should use CT

scanners that meet quality standards equivalent to or exceeding the accreditation standards of the ACR.<sup>55</sup> The original definition of a positive LDCT scan used in NLST was a nodule size of ≥4 mm, which was associated with a high percentage of false-positive results; studies suggest the need for alternate size thresholds and revision.<sup>11,99,349,350</sup> In v.1.2014 of the NCCN Guidelines for Lung Cancer Screening, the nodule size cutoff—to assign a positive result for solid and part-solid lung nodules on the initial LDCT screening—was increased to 6 mm from 4 mm used in earlier versions of the Guidelines.<sup>31,72,350,351</sup> Solid and part-solid lung nodules <6 mm on the initial LDCT screening scan are considered very low risk for lung cancer.

The Fleischner Society published guidelines for the management of incidentally detected solid pulmonary nodules on CT scans in 2005 followed by subsequent guidelines for subsolid nodules in 2013, which were harmonized into one guideline in 2017.<sup>245,251,352</sup> These guidelines are specifically for incidentally detected nodules and not for use in the lung cancer screening settings.<sup>353</sup> However, because of the familiarity and/or acceptance of Fleischner Society Guidelines among radiologists, pulmonologists, and thoracic surgeons, some of the principles were incorporated into the original NCCN recommendations for lung cancer screening.<sup>31</sup>

The ACR developed Lung-RADS specifically for the lung cancer screening population to provide a standardized reporting and management tool for clinicians. <sup>55,69,72,354</sup> Lung-RADS (and not Fleischner Society Guidelines) is recommended by the NCCN Guidelines, when interpreting CT findings in an individual who has undergone lung cancer screening, and for interval LDCTs performed for the management of screen-detected nodules. <sup>55,70,71</sup> Lung-RADS has been shown to improve the detection of lung cancer and to decrease the false-positive results to approximately 1 in 10 screened individuals compared with >1 in 4 in NLST. <sup>56,67,71,72,76</sup> For subsequent