CT Screening for Lung Cancer for High Risk Patients

- The recently published National Lung Cancer Screening Trial (NLST) showed that low-dose CT screening for lung cancer reduces mortality in high-risk patients
- However, screening results in a high rate of false-positive findings that require follow-up
- There are currently no national society guidelines regarding who should be screened
- Mass General Imaging offers CT screening for lung cancer, recommended in patients who meet the criteria used in the NLST
- CT screening for lung cancer is not covered by insurance

Lung cancer is the leading cause of cancer-related deaths. There is considerable evidence that if lung cancer is detected early, mortality is reduced. The National Lung Cancer Screening Trial (NLST), published in June 2011, demonstrated that lung cancer mortality in a high-risk population can be reduced by low-dose CT screening. Unlike prior studies that failed to show a benefit from screening, the NLST was a large prospective randomized clinical trial. The 53,454 participants (aged 55 to 74 years) all had a history of cigarette smoking of at least 30 pack-years and, if former smokers, had quit within the last 15 years. None had a history of cancer of any kind.

Individuals in the NLST trial were randomized to screening by low-dose CT or by radiography. Three exams were given: the first at baseline, the second one year after baseline and the third two years after baseline. The incidence of lung cancers was 645 cases per 100,000 person-years (1060 cancers) in the CT group and 572 cases per 100,000 person-years (941 cancers) in the radiography group (rate ratio, 1.13; 95% confidence interval, 1.03-1.23). The relative reduction in mortality (compared with radiography) from lung cancer with low-dose CT screening was 20%. The death rate from any cause in the CT screening group was reduced by 6.7%, compared to the radiography group. One death from lung cancer was prevented per 320 participants in screening.

Approximately 40% of the participants in the NLST had positive findings of small indeterminate pulmonary nodules considered suspicious for lung cancer in at least one of the three screening tests. These required diagnostic follow-up, mostly with further imaging and, in some cases, invasive procedures. Of these initial findings, 96.4% of the findings in the low-dose CT group were false positives. The rate of at least one complication during follow-up of the CT group was 1.4%. The rate of major complication was 0.06% in the false positive group and 11.2% in those with lung cancer. Of the cancers detected, most were adenocarcinomas, many of which were detected at stage I or stage II. Small cell lung cancers were, in general, not detected at early stages.

<table>
<thead>
<tr>
<th>Table 1. Selection Criteria for CT Screening for Lung Cancer</th>
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<td>Current and former smokers with a history of 30 pack-years of smoking*:</td>
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<td>- Former smokers must have quit within past 15 years</td>
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<td>55-74 years of age</td>
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<tr>
<td>No history of cancer within the past 5 years†</td>
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* A pack year equals the number of packs smoked per day multiplied by the number of years the patient smoked
† Patients with a history of cancer may qualify for routine CT studies
Figure 1. (A) Chest CT of a 70 year-old patient, a heavy smoker, revealed a 4 mm nodule (arrow) in right upper lobe. (B) Follow-up CT one year later shows the small nodule, increased in size. It was biopsied and then resected, revealing adenocarcinoma, papillary type.

**Indications for Lung Cancer Screening at Mass General Imaging**

Although the results of the NLST were positive, it is not clear how they translate to general clinical practice. National medical societies such as the American Cancer Society are developing guidelines for screening programs, but none are currently available.

Mass General Imaging now offers low-dose CT lung cancer screening. In the absence of national medical society guidelines, Mass General Imaging recommends using the same inclusion criteria used by the NLST, that is, patients aged 55 to 74 years who are current or former smokers with a history of 30 pack-years of smoking and who have no history of cancer within the past 5 years (Table 1).

Lung cancer screening CT studies must be ordered by a physician. The screening study is a non-contrast CT performed with a very low dose protocol with a radiation exposure of approximately 1.5 mSv. This is lower than that for a routine chest CT (about 3 mSv) and a fraction of some other CT scans. In comparison, typical annual background radiation from natural sources is 3.0 mSv in North America. The average radiation dose received from CT screening exams is likely to continue to decrease over time and may gradually become a less important issue.

Figure 2. Lung cancer detected by screening CT in a heavy smoker. (A) Low-dose screening CT shows a spiculated nodule in the right upper lobe (arrow). (B) FDG-PET confirmed (arrow) likelihood of cancer. The patient underwent biopsy and the nodule was found to be an adenocarcinoma.
Follow-up of Positive Findings

On screening CT, the finding of a small non-calcified pulmonary nodule (Figures 1 and 2) is regarded as suspicious for cancer and will require further evaluation. The current algorithm incorporating Fleischner Society guidelines for the evaluation of pulmonary nodules detected by CT imaging is shown in Figure 3. By definition, nodules found during CT screening for lung cancer fall in the category of nodules in patients with "No History of Cancer within the Past Five Years" and are in the "High Risk Category" highlighted in yellow in Figure 3. The selection of follow-up diagnostic imaging or procedure(s) and their timing depends on the size of the lesion and its morphologic characteristics, particularly if it has a "ground glass" or solid appearance.

Risk and Benefits

As the NLST trial demonstrated, screening does not prevent all deaths from lung cancer; it reduced the death rate by 20%. Screening also yields a high rate of false positive findings, some of which are incidental findings outside the lung. Although the vast majority of these findings are benign, they may result in unnecessary anxiety during follow-up care. For most patients, follow-up for indeterminate pulmonary nodules will be limited to non-invasive imaging, including CT or PET/CT, which will lead to additional cost and radiation exposure. Larger nodules may require needle biopsy, bronchoscopy, or video assisted thoracoscopic surgery (VATS) to establish the diagnosis and may lead to potential complications. The potential for adverse events associated with positive findings must be discussed with patients considering screening. While there is no insurance coverage for the screening CT scan, insurance should cover follow-up care for patients with positive findings. It should be emphasized that screening is not an alternative to smoking cessation, and active smokers undergoing screening CT should enter a smoking cessation program.
Scheduling

Appointments for low-dose CT for lung cancer screening can be scheduled by calling 617-724-9729 or through the Radiology Order Entry system, http://mghroe. The screenings are performed at the Mass General Imaging Centers in Chelsea, Waltham, and Worcester only and are not covered by insurance. The patient will be charged $350, due at the time of the screening examination. It is important that a responsible health care provider manage follow-up care for patients with a positive finding. Follow-up imaging examinations, which are covered by insurance, can be performed at the Mass General imaging centers or the main hospital campus.

A consultation for PNAB of the lung can be requested by calling Thoracic Imaging and Intervention at 617-724-4254 or by faxing a Thoracic Biopsy Approval form (PDF) to 617-724-0046, available on the Mass General Imaging website.

The Mass General Tobacco Treatment Service provides counseling on tobacco cessation. For more information, please call 617-726-7443.

Further Information

For more information about imaging CT screening for lung cancer, please contact Jo-Anne O. Shepard, MD, Director of Thoracic Imaging, Mass General Hospital, at 617-724-4256.

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References


PULMONARY NODULE FOUND ON X-RAY OR CT¹ ≥ 35 YRS OF AGE

COMPARISON WITH OLD STUDY CXR OR CT

If growth, consider Diagnostic Intervention PNAB⁶ or VATS⁶

Solid nodule, No growth > 2 yr¹²

No action²

Benign calcification or fat

Nodule, any size

CT

No history of malignancy within 5 years¹¹,¹²,¹³

Consider PNAB⁶, VATS⁶ or PET⁴ Attention to part solid/ground glass nodule³

≥ 35 YRS OF AGE

NO STUDY AVAILABLE

History of malignancy within last 5 years¹²

Follow-up CT at 3, 6, 12 and 24 months or according to clinical protocol

If growth, consider Diagnostic Intervention PNAB⁶ or VATS⁶

Suspect Infection, Immunocompromised/or fever¹²

Or consider Diagnostic Intervention PNAB⁶, Bronchoscopy or VATS⁶

Short term follow-up, ≤ 4-6 weeks and to resolution

If lesion resolves, No action

FOOTNOTES
1. An incidental pulmonary nodule is defined as a rounded opacity in the lung <3cm in size. The recommendations refer to solid pulmonary nodules unless otherwise specified. Nodule measurements are obtained in the long axis.
2. Non-solid (ground glass) nodules may require longer follow-up to exclude indolent adenocarcinoma.
3. Part solid / part ground glass nodules may be more aggressive carcinomas and may require earlier diagnostic intervention.
4. Bronchioloalveolar carcinomas (BAC), well-differentiated adenocarcinomas, and tumors <8mm may be FDG-PET(-). Granulomatous and inflammatory lesions may be FDG-PET(+).
5. Percutaneous needle aspiration biopsy (PNAB)
6. Video assisted thoracoscopic surgery (VATS)
7. History of smoking or of other known risk factors, including lung cancer screening patients
8. Minimal or absent history of smoking and of other known risk factors
9. The risk of malignancy in this category (<1%) is substantially less than that in a baseline CT scan of an asymptomatic smoker.
12. All follow-up imaging intervals are measured from the baseline scan timepoint.
13. Follow-up CT scans may be preformed with low dose CT protocols.