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Radiation Risks in Lung Cancer Screening Programs

A Comparison With Nuclear Industry Workers and Atomic Bomb Survivors

Robert J. McCunney, MD, MPH; and Jessica Li, BS

The National Lung Cancer Screening Trial (NLST) demonstrated that screening with low-dose CT (LDCT) scan reduced lung cancer and overall mortality by 20% and 7%, respectively. The LDCT scanning involves an approximate 2-mSv dose, whereas full-chest CT scanning, the major diagnostic study used to follow up nodules, may involve a dose of 8 mSv. Radiation associated with CT scanning and other diagnostic studies to follow up nodules may present an independent risk of lung cancer. On the basis of the NLST, we estimated the incidence and prevalence of nodules detected in screening programs. We followed the Fleischner guidelines for follow-up of nodules to assess cumulative radiation exposure over 20- and 30-year periods. We then evaluated nuclear worker cohort studies and atomic bomb survivor studies to assess the risk of lung cancer from radiation associated with long-term lung cancer screening programs. The findings indicate that a 55-year-old lung screening participant may experience a cumulative radiation exposure of up to 280 mSv over a 20-year period and 420 mSv over 30 years. These exposures exceed those of nuclear workers and atomic bomb survivors. This assessment suggests that long-term (20-30 years) LDCT screening programs are associated with nontrivial cumulative radiation doses. Current lung cancer screening protocols, if conducted over 20- to 30-year periods, can independently increase the risk of lung cancer beyond cigarette smoking as a result of cumulative radiation exposure. Radiation exposures from LDCT screening and follow-up diagnostic procedures exceed lifetime radiation exposures among nuclear power workers and atomic bomb survivors. ***CHEST 2014; 145(3):618–624***

Abbreviations: ERR = excess relative risk; ERR/Sv = excess relative risk of lung cancer associated with radiation dose; FNAB = fine-needle aspiration biopsy; LDCT = low-dose CT; NLST = National Lung Cancer Screening Trial

Lung cancer is the leading cause of cancer death worldwide. Despite treatment advances, 5-year survival rates from 1995 to 2001 were about 15.7%. Major risks of lung cancer include cigarette smoking and exposure to asbestos and other occupational agents, such as crystalline silica, hexavalent chromium, and arsenic.[1]

In the late 1990s, screening programs using low-dose CT (LDCT) scanning offered the promise of detecting early stage lung cancer. These early observational studies were limited, however, by the absence of control groups.

In 2011, a prospective assessment of 50,000 individuals that compared annual LDCT scan with annual chest film screening noted a decrease in mortality from lung cancer (20%) and all-cause mortality (7%) among those in the LDCT scan group.[2] The results led the

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American College of Chest Physicians and the American Society of Clinical Oncology to recommend annual screening with LDCT scan "for smokers and former smokers aged 55 to 74 years who have smoked for 30 pack-years or more and either continue to smoke or have quit within the past 15 years."[3] These are the first organizational recommendations advocating lung cancer screening; however, the recommendations are specific to the same entry criteria for participation in the National Lung Screening Trial (NLST).

What remains unclear, however, is how to evaluate potential benefits and risks of screening associated with other entry criteria. For example, will reduced lung cancer mortality be associated with younger ages at entry to screening or for lower pack-years of smoking than the 30-pack-year criteria of the NLST? In addition, articles have raised concern about ionizing radiation exposure risks associated with long-term lung cancer screening programs and the corresponding follow-up diagnostic studies.[4,5] The high percentage of nodules detected during prevalence and incidence screening and the need to evaluate these nodules with full-chest CT scanning (and corresponding higher radiation exposure than LDCT scanning) and diagnostic interventions, such as fine-needle aspiration biopsy (FNAB), may increase cumulative radiation exposure. The rate of nodules that prove to be false positive has ranged from 96% to 98%.[6-9] In the NLST, 96.4% of nodules detected were false positives not reflective of lung cancer.[2]

The need to follow up nodules detected on LDCT screening has raised the issue of the cumulative radiation dose that screening participants may encounter in both the screening and the diagnostic follow-up studies. In combination with periodic LDCT scans, these additional sources of radiation exposure could present an independent risk of lung cancer.

We determined ranges of cumulative radiation exposure a person may experience over 20- and 30-year periods by including both the screening LDCT scan and the follow-up diagnostic studies. We then contrasted the cumulative radiation exposures in screening programs with results of nuclear power plant workers and atomic bomb survivors.

Manuscript received June 19, 2013; revision accepted September 2, 2013.
Affiliations: From the Department of Biological Engineering (Dr McCunney and Ms Li), Massachusetts Institute of Technology, Cambridge, MA; and Brigham and Women's Hospital (Dr McCunney), Harvard Medical School, Boston, MA.
Correspondence to: Robert J. McCunney, MD, MPH, Department of Biological Engineering, Massachusetts Institute of Technology, 77 Massachusetts Ave, Room 16-771, Cambridge, MA 02139; e-mail: mccunney@mit.edu

DOI: 10.1378/chest.13-1420

Nuclear worker studies allow for an assessment of chronic low-dose radiation exposure, whereas atomic bomb survivor studies address acute high-dose exposure in people now followed over many decades. Nuclear worker studies offer advantages in this assessment because (1) the exposure pattern is generally chronic and low dose, (2) exposure data among nuclear workers have been closely documented, and (3) prospective studies have evaluated large cohorts (> 400,000 participants) over long periods of time and from many countries.[10] Atomic bomb survivor studies address health consequences of acute high-dose radiation exposure among people followed over 50 years. We considered the range in prevalence of nodules detected in LDCT screening and radiation doses associated with LDCT scan, chest CT scan, and FNAB in light of recommended Fleischner guidelines for follow-up of pulmonary nodules.[11] The purpose of the present report is to assess potential chronic radiation exposure in long-term (20-30 years) lung cancer screening programs and to assess the corresponding independent risk of lung cancer from radiation.

Materials and Methods

The NLST was used as the primary lung cancer screening reference because recommendations for screening by the American College of Chest Physicians and the American Society of Clinical Oncology have been based on this study.[2,3] Participants were aged 55 to 74 years, had a ≥ 30-pack-year smoking history, and were current smokers or former smokers who quit in the past 15 years.

Screenings yielding noncalcified nodules > 4 mm necessitated diagnostic follow-up, with full CT scan initially. The size of the nodule is the primary factor affecting the type of diagnostic follow-up.[12] According to the Fleischner guidelines, full CT scan is recommended for noncalcified nodules ranging in diameter from 4 to 8 mm, whereas FNAB is used for nodules > 8 mm[11] (Table 1).

To assess radiation exposure among LDCT scan screening participants, we approximated the range of nodules detected in both prevalence and incidence screening as 25% to 50% on the basis of a review of longitudinal studies of lung cancer screening with low-dose CT scanning. We used the follow-up of nodules as recommended by the Fleischner Society and considered lung cancer screening participants in the high-risk category.

Assumptions on the Prevalence and Incidence of Nodules Detected in Lung Cancer Screening

Up to 50% of smokers aged > 50 years have pulmonary nodules.[11,13] A significant heterogeneity has been noted in the percentage of nodules detected at incidence and prevalence in lung cancer screening programs. We chose to use the range of 25% to 50% for both incidence and prevalence of nodules detected on LDCT scan on the basis of several studies.[2,3,6,8,9] Incidence of nonpulmonary conditions warranting follow-up averaged about 5% in lung cancer screening programs.[9]

Radiation Doses From LDCT Scanning and CT Scanning

Radiation exposure is measured by a number of units, including sieverts and grays. The sievert reflects the effective dose and represents the stochastic biologic effects of ionizing radiation. One