Results of largest randomized lung cancer screening trial demonstrate screening with low-dose CT reduces death from lung cancer compared to chest X-ray

Philadelphia—Results of the National Lung Screening Trial (NLST) published online in today’s New England Journal of Medicine report a twenty percent reduction in lung cancer deaths among study participants who were screened with low-dose helical computed tomography (CT) versus those screened with chest X-ray. Conducted by the American College of Radiology Imaging Network (ACRIN) and the National Cancer Institute’s Lung Screening Study Group, the NLST enrolled 53,000 current and former heavy smokers aged 55 to 74 at 33 sites across the United States.

Lung cancer is the leading cause of cancer-related deaths in the United States, with more than 94 million current or former smokers at elevated risk of the disease. Most lung cancers are detected when they cause symptoms, by which time the disease is more likely to be advanced and less curable.

“The trial results published today provide hard evidence of the mortality benefit from low-dose helical CT screening for lung cancer in an older and heavy smoker population. These findings, and the vast amount of additional data generated by the NLST that are still being studied, offer a rich resource of information that will inform the development of clinical guidelines and policy recommendations,” states Denise R. Aberle, M.D., the national principal investigator for NLST ACRIN, a deputy co-chair of ACRIN, professor of radiology and bioengineering and vice chair for research in Radiological Sciences at UCLA.

The nearly decade-long trial, sponsored by the National Cancer Institute, a part of the National Institutes of Health, enrolled participants over a 20-month period who were randomly assigned to receive three annual screening examinations with either low-dose helical CT or standard chest X-ray.

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The paper published today provides important details about the number of screens that identified abnormalities potentially related to lung cancer and how many abnormalities were ultimately found to be cancer. The authors report, “During the screening phase of the trial, 39.1 percent of participants in the low-dose helical CT arm and 16.0 percent of those in the chest X-ray arm had a positive screening result. Across all three screening examination rounds, when a positive result was found, 96.4 percent of the low-dose helical CT and 94.5 percent of the chest X-ray examinations were false-positive.” William C. Black, MD, chair of the ACRIN Outcomes and Economics Committee and NLST site principal investigator at Dartmouth-Hitchcock Medical Center comments, “The follow-up for positive screening examinations most frequently involved further imaging tests and the data show that follow-up with invasive procedures was uncommon. We also found that lower rates of follow-up resulting from a positive scan occurred at later screening rounds.” The vast majority of false-positive results were probably due to the detection of normal lymph nodes or inflamed tissues.

Adverse events (harms resulting from the actual screening examinations) were few and relatively minor in the NLST. The rate of complications among participants who underwent a diagnostic evaluation prompted by a positive screening was under 2 percent for either type of screening.

“Although the NLST provides definitive evidence about the effectiveness of low-dose helical CT screening for lung cancer, significant further work is required to answer questions critical for the development of public policy recommendations,” says Constantine Gatsonis, Ph.D., the director of the ACRIN Biostatistics and Data Management Center, and chair of biostatistics in the public health program of the Warren Alpert Medical School of Brown University. Additional studies based on NLST data—to include the use of statistical modeling—will determine important information about which patient risk profiles, screening regimens and positive screen criteria result in the greatest screening benefit. As Gatsonis emphasizes, “Given the considerable costs associated with low-dose helical CT screening, a cost-effectiveness analysis using the NLST data is underway that will guide decisions about the best use of finite health care resources.”

The NLST also provided a unique opportunity to advance investigation of molecular biomarkers for the early detection of lung cancer. Specimens of blood, sputum and urine collected at ACRIN sites are banked in the NLST-ACRIN Biorepository, as are specimens of early-stage lung cancer, all obtained with consent from NLST participants. This resource is available to the larger research community. “These specimens provide a rich resource to validate molecular markers that may complement imaging to detect early lung cancer,” says Aberle. “By coupling biospecimen collection with imaging-based screening, the NLST-ACRIN Biorepository is relatively enriched for early clinical-stage lung cancers and associated biospecimens, and provides a unique resource of extremely well-characterized biospecimens with longitudinal data.”

“The knowledge that low-dose CT is a viable screening tool for detecting lung cancers at a curable stage is a tremendous first step for better understanding its implications for clinical care. Working with the Eastern Cooperative Oncology Group through the recently announced alliance, will allow us to extend these significant results to answer future questions critical for translating today’s findings into clinical practice,” says Mitchell D. Schnall, M.D., Ph.D., ACRIN’s network chair and the Matthew J. Wilson Professor of Research Radiology at the University of Pennsylvania.

“Furthermore, ACRIN is engaged in a research project with Boston University funded by the United States Department of Defense to investigate the role of blood and sputum-based laboratory tests to
better define patient populations who would most benefit from lung cancer screening and, thereby, reducing false-positive screenings.”

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For interviews with ACRIN-NLST investigators or an investigator at an ACRIN-NLST participating site, please contact Shawn Farley (703.648.8936; PR@acr.org)

ACRIN, a member of the NCI Clinical Trials Cooperative Group program, is made up of investigators from over 100 academic and community-based facilities in the United States and abroad. ACRIN’s oncology mission is to develop information through clinical trials of medical imaging with the potential to increase the length and quality of life of cancer patients. As recently announced, the oncology research agendas of ACRIN and the Eastern Cooperative Oncology Group are soon to be merged, with biomarker research as a central focus. ACRIN also carries out research through its cardiovascular and neuroscience committees. Its imaging core laboratory supports the imaging operations of the ACRIN enterprise as well as other organizations carrying out imaging research. ACRIN is headquartered at the ACR Clinical Research Center in Philadelphia, PA. The ACRIN Biostatistics Center is located at Brown University in Providence, RI.