



## Computed tomography screening of smokers for lung cancer can reduce deaths

*It has been reported that using computed tomography scans to screen current or former smokers can reduce deaths from lung cancers by 20%.*

The National Lung Screening Trial (NLST) was carried out at 33 National Cancer Institute (NCI) centers and involved over 53,000 current and former smokers. Participants were aged between 55 and 74 years and were studied for the effectiveness of low-dose helical computed tomography (CT) and standard chest x-ray as screening methods.

“Overall this study provides strong evidence that older patients who are at high-risk of developing lung cancer could benefit from CT screening and that’s a significant finding,” comments Claudine Isaacs, lead investigator of the NLST study at Lombardi Comprehensive Cancer Center, a part of Georgetown University Medical Center (DC, USA). “We are grateful to all the men and women who participated in this important study. Clinical trials are critical to making progress in medicine.”

“These results are very encouraging,” says Louis Weiner, director of Lombardi. “Studies like these generate so much excitement, but clearly there is much more work to be done. Lombardi and other NCI-cancer centers continue to explore effective ways to reduce lung cancer deaths including prevention efforts and by conducting clinical trials with the newest available cancer fighting drugs.”

In August 2002, the NLST study started to enroll participants with a smoking history of at least 30 pack-years, the average number of packs of cigarettes smoked per day multiplied by the number of years for which a person has smoked. These individuals could either be current or former smokers without signs, symptoms or a history of lung cancer.

Each individual was assigned to receive annual screens, over 3 years, of either CT or chest x-ray. The first screen was carried out at the time of enrolment, with participants receiving two further screens at 2 and 3 years postenrolment. Subsequent to this, each individual was followed up for a further 5 years with all deaths documented. A total of 354 deaths caused by lung cancer had occurred in the CT group by 20th October 2010. However, 442 lung cancer deaths occurred in the x-ray group; a significantly greater number.

“Potentially, we could save thousands of lives with CT screening, but keep in mind that because smoking causes many lung cancers, we could save hundreds of thousands more if people wouldn’t smoke or quit if they do,” Isaacs points out.

“We’re proud to be a part of this important study designed to answer critical questions,” says Howard J Federoff, executive vice president for health sciences at GUMC and executive dean of its School of Medicine. “Lombardi’s leadership role in the effort to reduce the burden of cancer has an impact at the national and local levels, and benefits our community directly.”

“This large and well-designed study used rigorous scientific methods to test ways to prevent death from lung cancer by screening patients at especially high risk,” said Harold Varmus, NCI Director. “Lung cancer is the leading cause of cancer mortality in the U.S. and throughout the world, so a validated approach that can reduce lung cancer mortality by even 20 percent has the potential to spare very significant numbers of people from the ravages of this disease.”



However, there are disadvantages of this approach. There is the potential for the cumulative effects of radiation to affect those being screened and there could be complications in patients who may not have lung cancer but need further tests to confirm this. In addition, the test may produce findings that are indicative of, but do not turn out to be cancer, and

this is likely to cause anxiety in patients. The disadvantages of CT screening in current and former smokers are issues that must be weighed up against the significant reduction in lung cancer deaths that can be achieved using this strategy.

Source: Georgetown University Medical Center: <http://gumc.georgetown.edu>

## Trial finds endosonography more effective than mediastinoscopy for mediastinal nodal staging of lung cancer

The results of a clinical trial comparing two different lung cancer staging strategies, endosonography and mediastinoscopy, were recently published in the *Journal of the American Medical Association*. The trial was carried out because staging of lung cancer holds prognostic value and is, therefore, an important aspect of patient care.

The current recommendation for patients with resectable non-small-cell lung cancer (NSCLC) is mediastinal nodal staging. However, surgical staging has limitations that result in the performance of unnecessary thoracotomies, a procedure that has a high risk of adverse effects on patient health. An acknowledged alternative to mediastinoscopy is endosonography (combined transesophageal and endobronchial ultrasound), a minimally invasive technique that can be followed by surgical staging if no nodal metastases are found.

The recent randomized controlled multicenter trial was conducted between

February 2007 and April 2009 in 241 patients with resectable NSCLC, in whom mediastinal staging was indicated based on computed tomography or PET. Of the 241 NSCLC patients involved in the trial, 118 were subjected to surgical staging while 123 underwent endosonography. Among the endosonography group, 65 patients subsequently experienced surgical staging. When there was no evidence of mediastinal tumor spread, thoracotomy with lymph node dissection was performed.

The researchers, led by Jouke T Annema, found the sensitivity of surgical staging was 79% (95% CI: 66–88%), whereas the sensitivity of endosonography alone was 85% (95% CI: 74–92%) and endosonography followed by surgical staging was 94% (95% CI: 85–98%). The number of unnecessary thoracotomies in the surgical staging group was 18%, while only 7% of patients experienced unnecessary thoracotomies in the endosonography group.

In addition to the improved sensitivity achieved with endosonography, it is cost effective compared with surgical staging and is typically preferred by patients as it does not involve a general anesthetic. Furthermore, researchers discovered that endosonography results in a lower complication rate (1 vs 6% for mediastinoscopy).

The researchers concluded that a staging strategy combining endosonography and mediastinoscopy was more sensitive and led to fewer unnecessary thoracotomies as compared with surgical staging alone. It is hoped that these promising results will alter the current recommendations such that endosonography becomes the first step in mediastinal nodal staging for resectable NSCLC patients.

Source: Annema JT, van Meerbeeck JP, Rintoul RC et al.: *Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: a randomized trial*. *JAMA* 304(20), 2245–2252 (2010).

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## Inhalable powder treatment for lung cancer shows promise

*Research presented at the 2010 International Pharmaceutical Federation Pharmaceutical World Congress suggests that a novel inhalable dry powder treatment is less invasive than other treatment options, such as radiation and surgery, and demonstrates an increase in survival rates.*

The dry powder was developed by Raimar Löbenberg and his colleagues Warren Finlay and Wilson Roa from the University of Alberta (AB, Canada) by encapsulating a common chemotherapy drug into nanoparticles.

The researchers demonstrated that the new treatment was more effective than using intravenous injection or a solution. In a mouse model, more than 80% of mice survived for 90 days and more than 70% survived for 140 days. This survival rate can be compared with the mice in the intravenous or solution groups, of which none survived for more than 50 days.

According to the Centers for Disease Control and Prevention, lung cancer accounts for more deaths than breast, prostate and colon cancer combined, and is the second-most common type of cancer in the USA. The majority of patients suffering

from lung cancer undergo multiple types of cancer treatment, which can each last for weeks or months.

In addition, the powder was more effective in reducing the amount and size of tumors compared with the intravenous injection or the solution, with mice that received the powder treatment demonstrating fewer and smaller tumors.

“Current lung cancer treatments can be grueling and take a significant toll on the patient,” said Löbenberg. “Our results show that this treatment method may not only increase someone’s survival rate but could also potentially be less toxic to the body.”

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Sources American Association of Pharmaceutical Scientists: [www.aaps.org](http://www.aaps.org); Centers for Disease Control and Prevention: [www.cdc.gov/cancer/lung/](http://www.cdc.gov/cancer/lung/)

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## Should lung cancer in smokers and never smokers be studied separately?

According to a recent pilot study, which was presented at the American Association for Cancer Research (AACR) Frontiers in Cancer Prevention Research Conference in November, lung tumors in individuals who smoke have different DNA alterations in their tumor genomes compared with people who do not smoke.

It has been proposed by Kelsie Thu, a PhD candidate at the BC Cancer Research Center in Vancouver (BC, USA), that lung tumors in smokers and never smokers may correspond to two different diseases. She suggested that, “lung cancer in never-smokers should be studied as a separate group.”

In an attempt to improve the present understanding of lung cancer development,

Thu and coworkers studied the biology of the disease to discover how it is different in patients who have never smoked compared with 53 patients who smoke or were smokers previously.

“A better understanding of the biology underlying lung cancer development will lead to improved detection and therapeutic strategies, and ultimately, will result in improved patient prognosis,” she said.

The researchers used genomic techniques to discover there were regions of DNA that were mutated in both the smoker and never smoker groups, but there were also regions of DNA that were altered preferentially in each specific group.

According to the study, as well as having more EGF receptor mutations – a

common finding – never smoker tumor genomes had more DNA mutations, in total, than those of smokers, indicating a higher degree of genomic instability and suggesting that tumors from never smokers could develop through separate mechanisms.

Thu describes the implications of their work, “Hopefully, our findings will stimulate the research community to further investigate the differences between lung cancer in these two cohorts, which could ultimately lead to the discovery of novel molecular targets for the diagnosis and treatment of lung cancer in never smokers”.

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Source: American Association for Cancer Research: [www.aacr.org](http://www.aacr.org)