National Cancer Institute

NLST NEWSLETTER

American College of Radiology Imaging Network Fall 2008

Tissue Testing Provides Insight into Lung Cancer

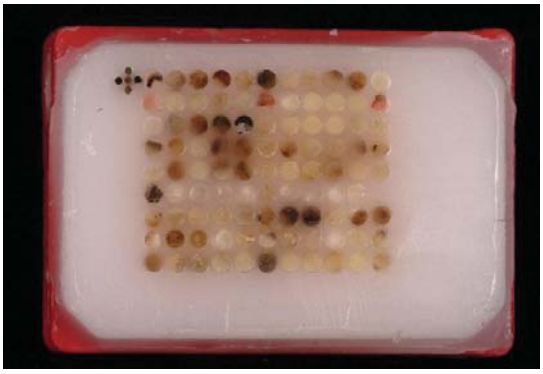
Information from the NLST follow-up forms is allowing scientists to perform important new research that may help them develop better tests for lung cancer in the future. This research may also help determine the kinds of individual therapies that may be best for a given patient.

Inside

Scientists are very interested in studying the tissues removed, or "resected," from people who have lung cancer to find out the differences in molecular make-up of lung cancers and how these differences affect their response to treatment. In the NLST, participants who have been diagnosed with lung cancer in which a part of the tumor has been removed are a major resource for better understanding lung cancer.

Most NLST participants signed a consent form during the general consent process for the NLST at the beginning of the trial to allow the collection of tissue for research. However, because the consent process varies from institution to institution, some participants may be contacted by their NLST site representative to seek permission.

If a participant agrees to the tissue research, researchers obtain a sample of the resected tissue from the pathology laboratory, which is sent to the UCLA Tissue Array Core Facility. The tissue sample is used to create what is called a tissue microarray. This involves taking many small samples, or cores, from the tissue sample to analyze the tumor without using all of the tissue. Once these microarrays are created, the larger, original tissue sample is returned to the pathology laboratory. Researchers can then perform many different tests on the microarrays. Both NLST and other researchers will be eligible to request the use of these tissues, but they will be required to submit a formal proposal. All proposals will undergo a formal review by an oversight committee consisting of experts from ACRIN, the scientific community, and the National Cancer Institute.



To create a tissue microarray, a hollow needle is used to remove tissue cores from tissues such as clinical biopsies or tumor samples embedded in paraffin. These tissue cores are then inserted in a different paraffin block in a precisely spaced, array pattern as shown above. Each microarray block can be cut into 100 - 500 sections, which can be used for independent tests. Common tissue microarray tests involve the analysis of cancer samples.

Researchers hope that these tests will help them find biological indicators for cancer called “biomarkers.” Examples of biomarkers include a unique protein or gene that is linked to a certain kind of cancer. Biomarkers have been an important focus of recent cancer research. The presence of specific biomarkers could better determine those people who are more likely to develop a disease such as lung cancer. Other biomarkers might be used to tailor treatment in individuals with lung cancer to a specific drug. Currently, the most widely used biomarker in cancer is the prostate-specific antigen (PSA), a protein that is present in the blood. High levels of PSA are associated with prostate cancer. Researchers would like to find more biomarkers associated with other kinds of cancer, including lung cancer.

"The NLST leaders thank our participants for returning their follow-up forms so that we can obtain important information about their cancer status," says Denise Aberle, MD, the NLST principal investigator. "We are grateful for their continued involvement in this study. NLST participants can know that they are part of a larger course of research with the potential to help many other people at risk for lung cancer in the future."

NLST Participant Plays Many Roles

To say that NLST participant Betty Lakey-Smith leads a busy life would be an understatement. For the past 30 years, Lakey-Smith, who lives in West Peabody outside of Boston, has done background work in Hollywood films, having appeared in such popular hits as "Indiana Jones and the Kingdom of the Crystal Skull," "The Departed," and "The Crucible." And with seven films under her belt this year, Lakey-Smith shows no sign of slowing down.

NLST Participant Betty Lakey-Smith

When asked how she got involved in this hobby, Lakey-Smith tells a story deserving a film of its own: "I got involved in this quite by accident. I was walking down the street to the hairdresser when I was stopped by casting director Billy Dowd. He wanted to cast me in one of his films and asked if I had an evening gown I could wear to Symphony Hall next Thursday." The rest is history.

Lakey-Smith learned about NLST from her doctor, who recommended that she participate. She continues to fill out follow-up forms by mail and says they "are not that time-consuming—there really isn't much to it."

A native of Hadleigh in Suffolk, England, Lakey-Smith enjoys traveling the globe, taking advantage of the flying privileges that came with her career as a customer service representative in the airline industry. A member of the Screen Actors Guild and the American Federation of Television and Radio Artists, she has two sons and six grandchildren, all of whom live in the Boston area. She enjoys vacationing in Fort Lauderdale, and while in Florida, she frequently volunteers at film festivals and art museums. "I came to Florida so that I could rest," she says, "and instead I got involved in more work!"

Radiation Exposure and NLST: Is there cause for concern?

Perhaps you remember that before you enrolled in the National Lung Screening Trial (NLST), you signed a document called an informed consent. That document informed you about many things regarding the NLST, including the potential benefits and risks of participation. Exposure to radiation was one of those risks. While radiation is known to increase the risk of cancer, the impact greatly depends on the amount of radiation (referred to as radiation dose) and the age at which a person is exposed. Furthermore, the impact of radiation exposure varies by body organ.

Although much research has been conducted on the impact of low-dose radiation exposure and cancer risk, controversy still remains as to whether such exposure meaningfully increases cancer risk. Both the CT and x-ray exams included in the NLST impart radiation exposure. However, the CT exams resulted in roughly 10 times greater exposure than the chest x-rays, even though "low-radiation-dose" CT scanners were used to minimize radiation exposure. While "10 times greater" may seem high, it's helpful to know that the CT scanners used in the NLST imparted about the same radiation exposure as a screening mammogram. NLST researchers believe that a potentially small, yet unproven, increase in cancer risk was outweighed by the possibility of a larger benefit with screening.

In November 2007, an article on cancer risk associated with CT exams was published in the *New England Journal of Medicine*. The authors estimated that typical CT exams could play a role in development of 1.5 to 2.0 percent of future cancers in the United States. NLST participants who heard of these findings may have wondered how to interpret them in light of their trial experience. Therefore, we are providing additional information about the methods the authors used to calculate radiation exposure.

The authors calculated exposure from diagnostic CT scanners that impart a radiation dose roughly two to three times higher than that received from CT scanners used in the NLST. Also, they calculated cancer risk using primarily the experience of the Hiroshima and Nagasaki atomic bomb blasts. Use of these data is common in radiation research; however, it is uncertain whether the data can be used to precisely measure the exact increase in risk from CT exam radiation.

Additionally, the authors calculated the percent of cancers that would have radiation exposure from a CT as a contributing cause (most cancers are not caused by only one exposure). This

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NLST Data Use Beyond Lung Cancer by Denise Aberle, MD

NLST researchers are beginning to explore several basic questions about lung cancer risk and smoking-related lung diseases. The National Lung Screening Trial is a tremendous source of information about lung cancer risk, of course, but it will also provide researchers with information about another disease related to smoking: chronic obstructive pulmonary disease (COPD).

COPD is a common complication of smoking. COPD is not one disease, but may be thought of as having two major components: chronic bronchitis and emphysema. Chronic bronchitis is characterized by thickening of the airways, which can then collapse during exhalation, obstructing the flow of air out of the lungs. Emphysema results from the destruction of lung tissue itself, resulting in the development of "holes" in the lungs, which decreases the lung's normal elasticity. With decreased elasticity, the airways collapse as an individual exhales. A patient with COPD usually has a mix of the two diseases rather than only bronchitis or only emphysema.

Scientists know that the presence of COPD, aside from smoking itself, is a risk factor for lung cancer. Recent studies also suggest that emphysema alone is a risk factor for lung cancer. The ACRIN NLST performed pulmonary function tests on subjects at the time of the baseline screening exams. The NLST screening examinations will be a powerful means to clearly define how much airway disease and emphysema are present in the lungs. Combined with pulmonary function tests, we hope to be able to better understand the differences between men and women in how they develop COPD or emphysema and how this influences their risks for lung cancer.

NLST Principal Investigator Denise Aberle, MD, promotes use of the NLST data to answer questions about a variety of lung-related diseases.

Radiation Exposure ***(continued from page 2)***

calculation then reflects the number of scans conducted in the US as a whole, rather than the increase in cancer risk to an individual receiving scans.

The NLST strives to determine whether screening using low-radiation-dose CT scanners provides a benefit for persons at risk for lung cancer. We're grateful that you are willing to help us find the answer.

This content is largely based upon an article appearing in the NLST Newsletter (Vol. 6, Issue 2) published by the Lung Screening Study component of the National Lung Screening Trial.

The F2 Form is on a Diet!

As an NLST participant, you are very familiar with the F2 form that requests information about your outpatient doctor visits, hospitalizations, and emergency room visits. This information allows the NLST investigators to learn about medical events that may be directly or indirectly related to the NLST screening exams.

We have heard from many of you that a shorter F2 form would be welcome. WE AGREE! The NLST investigators are in the process of revising the form and anticipate that the new form will take less than 5 minutes to complete - and the return postage is prepaid!

Be on the look out for a future F2 form update. Meanwhile, thank you for your continued dedication to this trial. The knowledge gained from NLST will be the single most influential information upon which future public health decisions about lung cancer screening are made.

Sponsored by the National Cancer Institute (NCI), the National Lung Screening Trial was carried out at more than 50 sites across the U.S. with coordination provided by both the NCI and the American College of Radiology Imaging Network (ACRIN).

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ACRIN™ American College of Radiology Imaging Network

National Cancer Institute

Cucumber Yogurt Dip

A healthy snack from recipes available on the Centers for Disease Control and Prevention (CDC) Web site: www.5aday.gov

Recipe Summary:

Preparation Time: 15 minutes

Number of Servings: 6

Cups of Fruits and Vegetables Per Person: 0.50

Ingredients:

- 2 cups plain low-fat yogurt
- 2 large cucumbers, peeled, seeded, and grated
- 1/2 cup nonfat sour cream
- 1 Tbsp lemon juice
- 1 Tbsp fresh dill
- 1 garlic clove, chopped
- 1 cup cherry tomatoes
- 1 cup broccoli florets
- 1 cup baby carrots

Directions:

Peel, seed, and grate one cucumber. Slice other cucumber and set aside. Mix yogurt, grated cucumber, sour cream, lemon juice, dill, and garlic in a serving bowl. Chill for 1 hour. Arrange tomatoes, cucumbers, broccoli, and carrots on a colorful platter. Serve with cucumber dip.