An Overview of how Novel AI-enhanced Blood Testing Technology can Diagnose Lung Cancers with High Accuracy Rates.

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Abstract

Lung cancer is one of the largest leading causes of cancer-related deaths worldwide, “accounting for the highest mortality rates among both men and women.”[1]. Lung Cancer is the abnormal growth of cells that grow in an uncontrollable way in the lungs [5]. According to the World Health Organization (2023), cancer incidence and mortality produced by the International Agency for Research on Cancer (IARC) show that lung cancer remains the leading cause of cancer death, with an estimated 1.8 million deaths (18%) in 2020 [1]. Despite the availability of treatments such as chemotherapy and radiotherapy, the cases of lung cancer continue to rise over time. This increase is due to factors like the development of resistance to treatments, delayed treatments, and new cancerous growth in previously treated individuals. The World Health Organization (2023), have established that early detection can increase the chances of successful treatment and improve outcomes [1]. Through the new advancements in the technology used for the detection of lung cancer, researchers at the Johns Hopkins Kimmel Cancer Center found a novel artificial intelligence blood testing technology that detected over 90% of lung cancers in samples from about 800 individuals with and without cancer [3]. This research paper serves as a comprehensive review on lung cancer, focusing on the new detection method which uses novel AI blood testing, while reviewing its etiology and preventions.

Introduction

Lung Cancer is one of the largest threats that results in the deaths of millions across the world. In the U.S., lung cancer is the leading cause of cancer deaths among both men and women. While the exact causes of lung cancer can vary, they often involve respiratory failure through tumor or complications like pneumonia, or from the effects of cancer treatment.

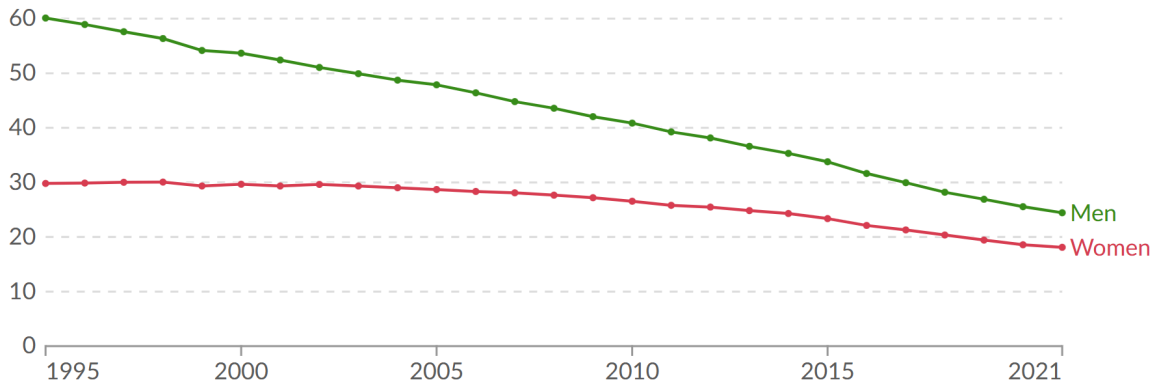

Fig. 1. The Reported annual death rate from lung, bronchus or trachea cancers per 100,000 people [8]

Although lung cancer mortality rates among both men and women decreased from 1995 to 2021, the annual death rate remains high, continuing to cause a significant public health challenge in these generations.

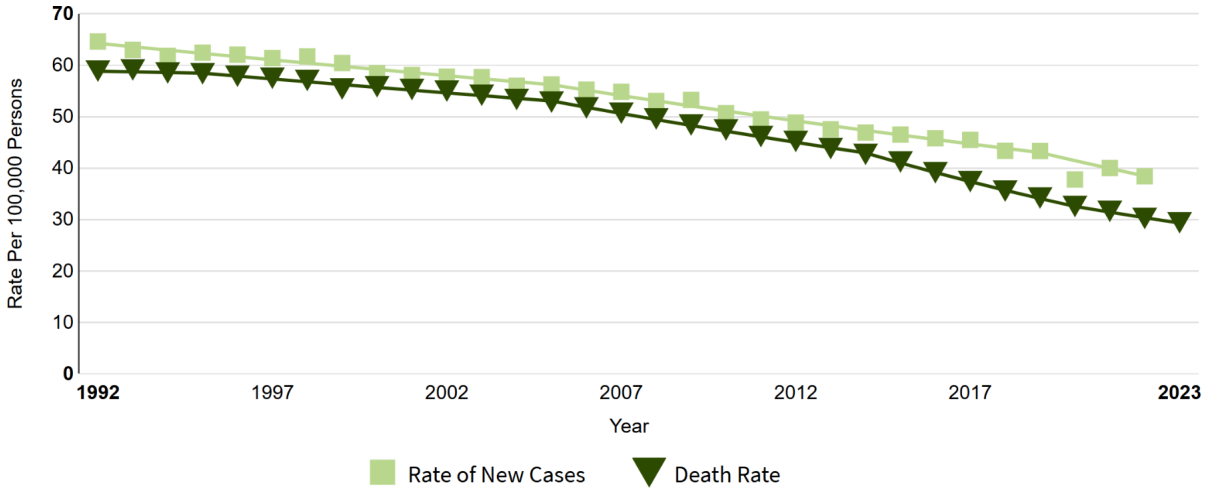

Fig. 2. New cases come from SEER 12. Deaths come from U.S. Mortality. Compares the rates of new cases and the death rate [7].

The graph illustrates the trends in the rate of new lung cancer cases and the death rate due to lung cancer in the United States from 1992 to 2023. While there is a decline in the amount of cases and deaths over the years, it is evident that the death rate remains significantly high. Even though the advancements in public health interventions have reduced the rate of new cases, lung cancer still continues to be the major cause of mortality. This can be attributed to many factors such as late-stage diagnosis, limited availability to early screening, and the aggressive nature of certain types of lung cancer. This is where novel AI-enhanced blood testing technology is used. The test approach, called DELFI (DNA evaluation of fragments for early interception), spots unique patterns in the fragmentation of DNA shed from cancer cells circulating in the bloodstream. Applying this technology to blood samples taken from 796 individuals in Denmark, the Netherlands and the U.S., investigators found that the DELFI approach accurately distinguished between patients with and without lung cancer [3].

Early detection is important in improving survival rate, as it increases the time when the cancer is more likely to be treated. According to the World Health Organization (2023), early detection can significantly increase the chances of successful treatment and improve outcomes [1]. By identifying lung cancer in its initial stages, AI-powered blood tests can reduce the number of individuals who experience more advanced, less-manageable and treatable stages of cancer.

What is Lung Cancer?

As mentioned before, lung cancer is the uncontrollable growth of cells in the lungs. People who smoke have the greatest risk of lung cancer and this increases with the length of time and number of cigarettes smoked [5]. Lung cancer also can happen in people who have never smoked. There are two main types of lung cancer: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).

About 80% to 85% of lung cancers are NSCLC. The main subtypes are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Adenocarcinoma originates in mucus-producing epithelial cells and is seen in both smokers and non-smokers, especially in women and younger individuals. Squamous cell carcinoma starts in flat cells lining the airways and is strongly associated with smoking, typically seen near the central parts of the lungs. Large cell carcinoma can develop in any part of the lung, it grows quickly, and is harder to treat. A subtype of large cell carcinoma is large cell neuroendocrine carcinoma, LCNEC, which behaves similarly to small cell lung cancer. Other rare NSCLC subtypes include adenosquamous and sarcomatoid carcinoma [6].

Another type of cancer is small cell lung cancer (SCLC). It makes about 10% to 15% of all lung cancer cases and is known for its rapid growth and spread. By the time it is diagnosed, it has usually spread beyond the lungs. While SCLC responds well to chemotherapy and radiation therapy due to its fast-growing nature, it is likely to return after initial treatment [6].

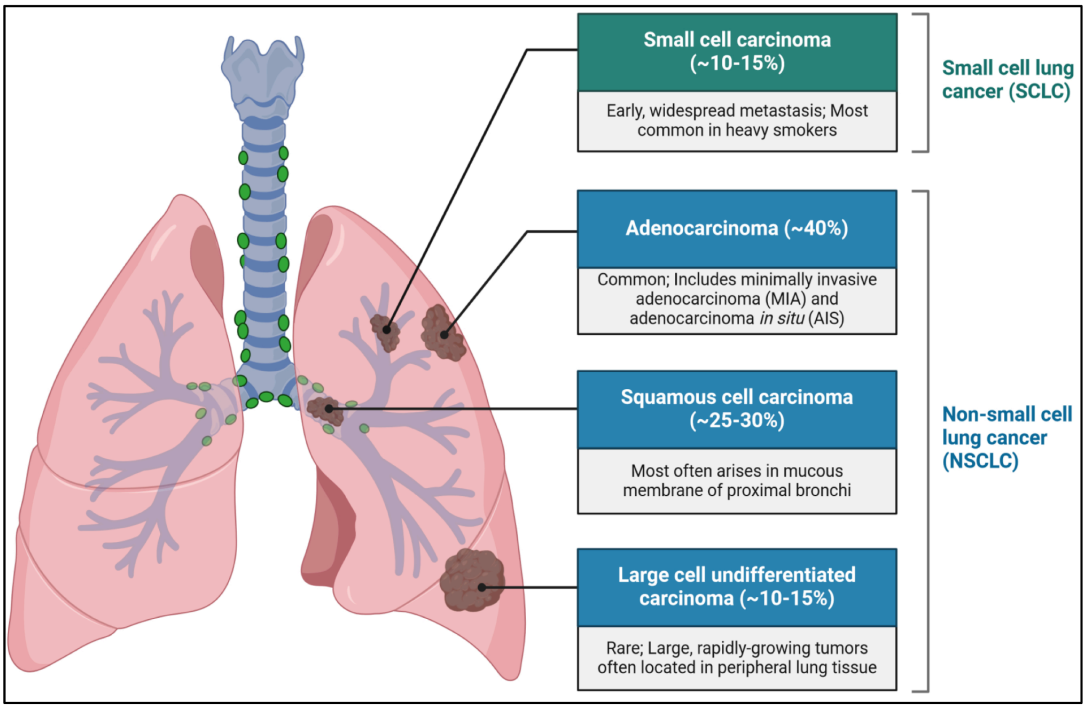

Fig. 3. This image illustrates the different types of lung cancer and summarizes their characteristics [9].

The Etiology and Risk Factors

Lung cancer takes place when the cells in the lungs experience changes in their DNA. In healthy cells, the DNA gives instructions to multiply and grow a set number of cells in a specific amount of time. But in cancer cells, the DNA changes tell the cancer cells to make many more cells causing the cancer cells to live while the healthy cells are harmed. Thus causing the uncontrollable growth of cancer cells. Cancer cells can spread to other parts of the body. When cancer spreads, it is called metastatic cancer [5].

Researchers believe smoking causes lung cancer by damaging the cells that line the lungs. Cigarette smoke is full of carcinogens which when you inhale, causes changes in the lung tissue. At first your body may be able to repair this damage. But repeated exposure can damage the lining of your lungs [5].

There are many factors that contribute to the risk of lung cancer. Some risks can be controlled while others cannot be controlled. The risk factors for lung cancer include smoking, exposure to secondhand smoke, previous radiation therapy, exposure to radon gas, exposure to cancer-causing substances, and family history of lung cancer [10].

Smoking is the leading cause, with the risk increasing based on the number of cigarettes smoked and the duration of smoking. Secondhand smoke also poses a significant risk to non-smokers. Other risk factors include previous history of chest radiation therapy, exposure to radon gas, and contact with carcinogenic substances such as asbestos, arsenic, chromium, and nickel, especially in the workplace. Additionally, a family history of lung cancer can raise one's risk [10].

Prevention

According to the World Health Organization (2023), the most effective way to prevent lung cancer is by not smoking tobacco, as smoking remains one of the leading causes of the disease [1]. It is also important to decrease the exposure to other risk factors such as secondhand smoke, which can harm non-smokers who are usually around people who smoke. Environmental and occupational exposures, such as air pollution and hazardous substances in the workplace, including chemicals like asbestos, arsenic, and other carcinogens, can increase the risk of developing lung cancer.

Lung cancer prevention involves primary and secondary strategies. Primary prevention aims to stop the disease before it starts [11]. This can be done through increasing healthy behaviors and reducing risk factors. Public health initiatives under primary prevention include enforcing smoke-free environments, applying strict tobacco control policies, conveying occupational safety standards, and reducing air pollution levels [1]. These efforts not only help individuals lower their personal risk but also contribute to a healthier environment and community.

On the other hand, Secondary prevention focuses on early detection of lung cancer, especially in individuals who are at high risk, such as long-term smokers or those with a history of significant exposure to harmful substances. The primary tool for early detection is low-dose computed tomography (LDCT), which can identify lung cancer in its early stages [11],[1].

By combining both primary and secondary preventions, such as encouraging healthy lifestyles, reducing environmental risks, and implementing effective screening programs, it is possible to make a substantial impact on lowering lung cancer incidence and mortality [1],[11].

Novel AI Blood Testing Technology Can Identify Lung Cancers with High Accuracy

Researchers at the Johns Hopkins Kimmel Cancer Center have developed a novel AI blood testing technology called DELFI (DNA evaluation of fragments for early interception) that has a high accuracy rate for identifying and detecting lung cancer. In a study involving about 800 individuals from Denmark, the Netherlands, and the U.S., the DELFI identifies patients with and without lung cancer with an overall detection rate above 90% [2],[3]. The DELFI technology analyzes the unique fragmentation patterns of DNA shed from cancer cells into the bloodstream. This approach provides a view of cell-free DNA referred to as the "fragmentome."[2],[3]. By combining DELFI with clinical risk factors, a protein biomarker, and follow-up imaging, the test detected 94% of lung cancer across all stages, including 91% of stage I/II and 96% of stage III/IV, at 80% specificity [4].

Lung cancer remains the leading cause of cancer-related deaths globally, claiming nearly 2 million lives every year, year fewer than 6% of at-risk Americans receive recommended low-dose computed tomography (LDCT) screening. This low screening uptake is due in part to concerns about potential harm from investigation of false positive imaging results, radiation exposure or worries about complications from invasive procedures [2],[3]. Victor E. Velculescu, the study’s senior author, emphasized the urgent need for alternative, noninvasive screening options that are safer and more accessible. Lead author Dimitrios Mathios highlighted that a blood test, or “liquid biopsy”, for lung cancer could be a good way to enhance screening efforts, because it would be easy to do, broadly accessible and cost-effective [2],[3]. The DELFI test does this by requiring only low-coverage genome sequencing, making it well-suited for large-scale screening programs.

The DELFI technology uses a blood test to indirectly measure the way DNA is packaged inside the nucleus of a cell by studying the size and amount of cell-free DNA present in the circulation from different regions across the genome. Healthy cells package DNA in a well-organized way in which different regions of the genome are placed carefully in different components, whereas cancer cells have disorganized DNA packaging that releases chaotic DNA fragments into the blood. By applying machine learning, DELFI identifies abnormal patterns of DNA fragmentation that are characteristics of cancer [2],[3]. This approach allows researchers to indirectly detect cancer by studying the “fragmentome” rather than relying only on direct tumor markers. Overall, DELFI offers a noninvasive, innovative way to screen for cancer with high accuracy.

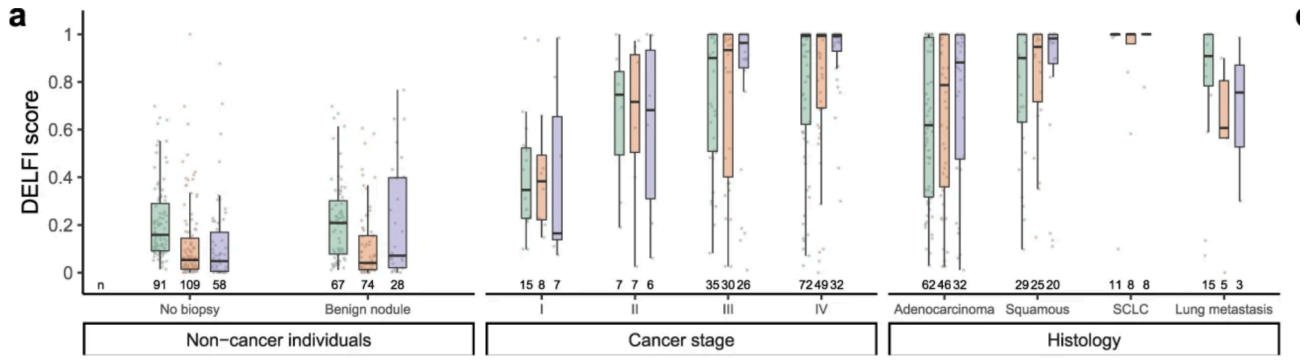

Fig. 4. Performance of DELFI analyses for lung cancer patients and non-cancer individuals [4].

This image illustrates the performance of DELFI analyses for lung cancer patients and non-cancer individuals. Different groups in the study are represented by green (all participants), orange (patients without prior cancer history), and blue (patients who meet a certain age and smoking history). The DELFI test scores for non-cancer patients are lower than those for cancer patients. These scores increase as cancer progresses to more advanced stages. The highest scores are seen in patients with small cell lung cancer (SCLC). The boxplots show median scores and the spread of scores in each group, with lines and whiskers showing how scores vary [4].

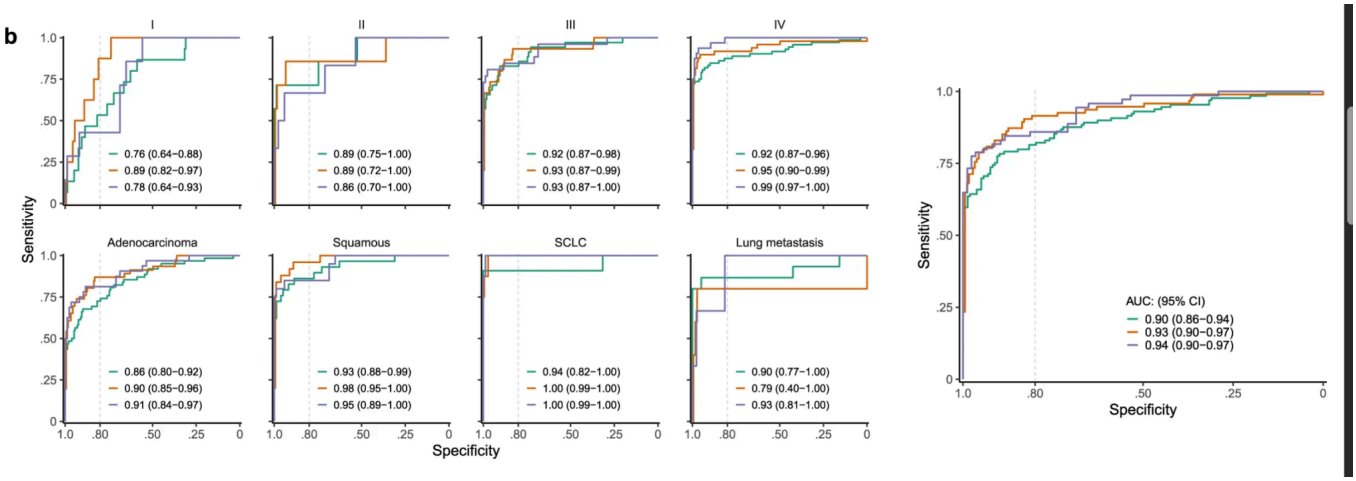

Fig. 5. This image represents the different specificities the DELFI test can distinguish between people with and without lung cancer [4].

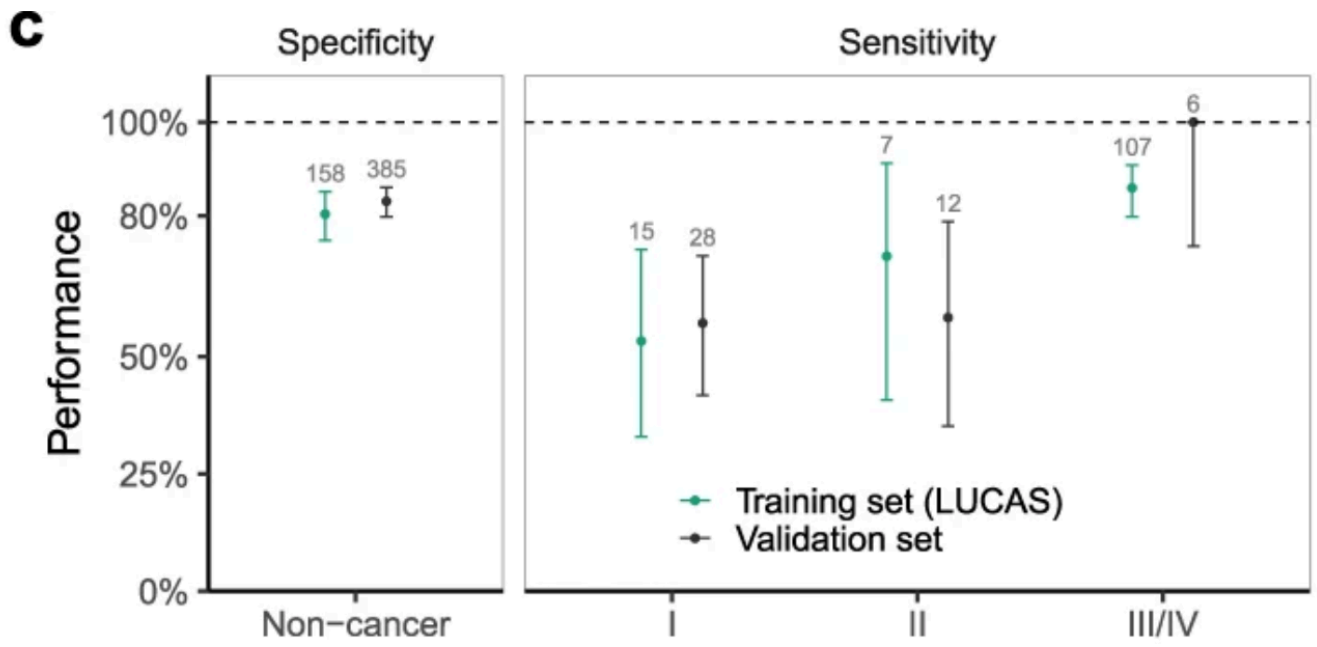

Fig. 6. This image illustrates the use of the training set and the validation set to compare the performance of the DELFI test [4].

The researchers used ROC (receiver operating characteristic) analyses to test how well the DELFI test can differentiate between people with and without lung cancer. These ROC curves were made for all patients together and then split by stage and cancer type. An 80% specificity mark was chosen as a reference point for making decisions about a positive test. This helps show how accurate the test is at different thresholds [4].

These images highlight the DELFI model's ability to detect lung cancer accurately and reliably. Increase with cancer stage, the boxplot shows that DELFI scores are higher in cancer patients than in non-cancer patients, this helps to identify early-stage cancers. The ROC curves show that the DELFI model has strong performance with a selected specificity threshold, showing its reliability in distinguishing cancer from non-cancer. The application of a consistent DELFI score cutoff to a separate validation group gives similar results, proving the model's consistency and validity across different patient populations. Overall, these visuals together demonstrate that the DElFI model is a powerful and accurate tool for early lung cancer detection.

Conclusion

Lung cancer remains the leading cause of cancer-related deaths worldwide, emphasizing the need for improved prevention, early detection, and treatment methods. Despite progress in treatment options, such as chemotherapy and radiotherapy, the high mortality rate continues due to factors like treatment resistance, delays in intervention, and recurrence of disease [1],[11]. This review highlights the transformative potential of a novel artificial intelligence based

blood testing technology developed by researchers at the Johns Hopkins Kimmel Cancer Center. The DELFI model, by analyzing cell-free DNA fragmentation patterns, has shown high accuracy rates in detecting lung cancer in both early and advanced stages. Implementing such innovative screening methods, alongside preventive measures and education, offers a way to reduce the global burden of lung cancer and improve patient outcomes [2],[3],[4].

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