



Lung Cancer – Early Detection Saves Lives

LungSign™ – A New Tool for Early Detection of Lung Cancer

About LungSign™

- An innovative marker for the early detection of lung cancer
- Safe, simple, non-invasive and painless
- Able to analyze lung cells found in sputum
- Able to identify individuals harboring early stage lung cancer

About Lung Cancer

- Initially can grow without symptoms
- Kills more people than any other type of cancer
- Survival rates have remained unchanged over the last 30 years
- However, 5 year survival rates greatly improve with early diagnosis

Who Should Consider LungSign™?

LungSign™ should be considered if you meet at least 2 of these 3 criteria:

- over 50 years old
- significant exposure to
 - cigarette smoke (1 pack or more for 20 years or more)
 - industrial carcinogens (e.g. asbestos)
- You have symptoms such as:
 - Persistent cough
 - Shortness of breath

Who Should Not Consider LungSign™?

- If you have had thoracic or cardiac surgery within the last 6 months
- If you have had an exacerbation of asthma or COPD (Chronic Obstructive Lung Disease) in the last 5 days
- If you have flu-like symptoms (chills, fever)
- If you have had radiation treatment or chemo therapy

Risk Factors

- Cigarette smoke (up to 85% of all lung cancers are caused by cigarette smoke)
- Exposure to environmental carcinogens (e.g.: asbestos, radon) and lung diseases which scar the lungs
- Age (>50) and heredity may contribute if other risk factors are present

How to order LungSign™

Three easy methods:

1. By phone (toll-free): **1.888.629.8779**
2. By email: **info@LungSign.com**
3. Online: **www.LungSign.com**

Note: a physician's requisition is required. Also, you may have to pay for this test directly \$225 (CAD).



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LungSign™ – New Hope for Early Detection of Lung Cancer

LungSign™ — How can it help me?

In the past, if you were worried about having lung cancer, there was no simple test to take. Most patients, even high-risk patients, were not tested for lung cancer until they showed symptoms of the disease. By then, if lung cancer was present, it was usually too late.

Fortunately, times have changed. LungSign™ has been designed to test for early-stage lung cancer in high-risk individuals:

- Over 50 years old
- Who have had significant exposure to:
 - cigarette smoke (one pack a day for 20 years) or
 - industrial carcinogens
- With symptoms such as persistent cough or shortness of breath or other indicators such as suspicious radiography

Battling cancer one test at a time

When it comes to lung cancer, early detection is key to extending lives and improving the quality of life for those who have the disease. LungSign™'s innovative technology brings new hope to the battle, with a safe, simple, non-invasive test for the early detection of lung cancer. By analyzing the lung cells commonly found in sputum, LungSign™ can detect cancer before it spreads, increasing the likelihood of successful treatment.

Similar to the Pap test for cervical cancer or the PSA test for prostate cancer, LungSign™ does not provide a “yes or no” diagnosis. Instead, LungSign™ indicates the likelihood that an individual has lung cancer.

Although not a diagnostic test, the existence of a likelihood predictor such as LungSign™ is potentially of enormous value in the fight against lung cancer.

Lung Cancer

According to the World Health Organization, lung cancer is a global problem, accounting for 1.2-million new cases worldwide every year. In North America, lung cancer kills more men and women than any other type of cancer. And in the developing world, the peak of this epidemic has yet to be seen.

Over the last 30 years, doctors have greatly improved the survival rates for many types of cancer. Sadly, lung cancer survival rates remain unchanged. Aggressive but silent, lung cancer typically grows without symptoms, not betraying its presence until it's too advanced to be cured.

The good news is that when lung cancer is detected early the chances for survival are greatly improved. Early detection of lung cancer offers patients the best hope for a favorable outcome.

Risk Factors for Lung Cancer*

Cigarette smoking is the primary risk factor for lung cancer. It is estimated that 85 percent of all lung cancer cases are caused by cigarette smoking. An individual's risk of developing lung cancer depends on how much they've smoked, the age at which they started smoking, and the age at which they quit.

For non-smokers, second-hand smoke is the main cause of lung cancer, but other risk factors include: exposure to industrial or environmental carcinogens such as asbestos and radon; and lung disease, especially diseases which scar or damage the lungs. The risk of developing lung cancer also increases with age and heredity.

* Canadian Cancer Society; <http://www.cancer.ca> November, 2006.



Taking the LungSign™ Test

The LungSign™ test is performed on sputum — the material brought up from the lungs by a deep cough.

The LungSign™ home test kit includes a simple, hand-held device which, when blown into, vibrates the chest to stimulate the production of sputum. The same vibrations painlessly shake sputum from the lung's lining, and help you cough deeply, to produce the sample necessary for LungSign™ analysis.

Taking the LungSign™ test causes very little physical discomfort. Almost anyone can take the LungSign™ test, with the following exceptions:

- patients who have had thoracic or cardiac surgery within the last 6 months
- patients with asthma or COPD (chronic obstructive lung disease) exacerbation in the last five days
- patients with flu-like symptoms such as fever or chills

Analysis

Once collected, sputum samples are sent to the Perceptronix laboratory for analysis, and are generally reported within two weeks.

LungSign™ Results

LungSign™ is not a diagnostic tool. It does not provide a definitive “yes or no” answer to the question: “Do I have lung cancer?” Instead, LungSign™ results are presented as a “risk multiplier,” indicating the statistical likelihood that an individual harbors lung cancer.

LungSign™ scores should be interpreted in context to an individual's overall health and

medical history. Therefore LungSign™ results are sent to your doctor, who has the expertise necessary to interpret them and recommend any further action.

Talk With Your Doctor

If you would like to take the LungSign™ test, talk with your doctor about your risk of lung cancer, and about whether or not the LungSign™ test is right for you.

Test Cost

LungSign™ has an introductory price of CAD\$225 and is not currently reimbursed by health care providers.

Perceptronix Medical Inc.


LungSign™ was developed by Perceptronix Medical Inc.

Perceptronix believes that early diagnosis is the key to improving outcomes for lung cancer patients. The company, a spin-off of the BC Cancer Agency (Vancouver, Canada), has worked collaboratively with scientists and clinicians from around the world to develop technologies that address the problem of early cancer detection.

The goal of Perceptronix is to create products and services that support the early diagnosis of cancer for better patient outcomes.

Information and Ordering

toll free: 1.888.629.8779
e-mail: info@LungSign.com
website: www.LungSign.com



*LungSign™ – A New Tool
for the Early Detection of
Lung Cancer*

LungSign™ At a Glance

LungSign™ Summary

- An innovative marker for the early detection of lung cancer
- Able to detect lung cancer even in the absence of cancer cells
- Able to detect changes in normal appearing cells associated with the presence of lung cancer
- Safe, simple, non-invasive, and painless
- Utilizes MAC (Malignancy Associated Changes) technology to analyze lung cells found in the sputum
- Requires a deep cough specimen – kits are provided for specimen collection
- Provides an assessment of the likelihood of the presence of cancer
- Complements the current Standard of Care

Lung Cancer Facts

- Initially can grow without symptoms
- Kills more people than any other type of cancer
- Lung cancer mortality exceeds the combined total of breast, colorectal and prostate cancer
- Survival rates have remained unchanged over the last 30 years
- However, 5 year survival rates greatly improve with early diagnosis (> 80% for stage 1 patients)

Candidates for LungSign™

Identified High risk patients:

- over 50 years old
- significant exposure to
 - cigarette smoke (1 pack or more for 20 years or more)
 - industrial carcinogens (e.g. asbestos)
- Also, patients presenting with symptoms such as:
 - Persistent cough
 - Shortness of breath/early diagnosis (> 80% for stage 1 patients)

Patient Disqualifications

The following would not be considered suitable candidates for LungSign™:

- Patients who have had thoracic or cardiac surgery within the last 6 months
- Patients with an exacerbation of asthma or COPD (Chronic Obstructive Lung Disease) in the last 5 days
- Patients with flu-like symptoms (chills, fever)
- Patients who have had radiation treatment or chemo therapy

High Risk Patient Identification

The goal is to identify at risk patients prior to the presentation of symptoms. The following are characteristics to identify such patients.

- Cigarette smoke (up to 85% of all lung cancers are caused by cigarette smoke)
- Exposure to environmental carcinogens (e.g.: asbestos, radon) and lung diseases which scar the lungs
- Age (>50) and heredity may contribute if other risk factors are present

How to order LungSign™

Three easy methods:

1. By phone (toll-free): **1.888.629.8779**
2. By email: **info@LungSign.com**
3. Online: **www.LungSign.com**

Note: a physician's requisition is required. You may wish to advise your patient that out of pocket payment is \$225 (CAD).



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Fax: 604-629-8786
Email: info@LungSign.com
Web: www.LungSign.com



Introducing LungSign™

LungSign™ is the first test to market to offer a safe, painless and convenient method of assessing a patient's risk of lung cancer. Based on an innovative marker for malignancy, LungSign™ is designed to detect cancer in its early, presymptomatic stages. LungSign™ also serves as a useful complement to current radiological diagnostic methods.

Engendered by research at the British Columbia Cancer Agency, LungSign™'s potential has been established through a multi-centered validation trial, which demonstrated that fully automated DNA analysis of sputum cells using LungSign™ detects Stage I cancer.

Lung Cancer — the Facts

According to the World Health Organization, lung cancer accounts for 1.2-million new cases worldwide every year. Lung cancer mortality exceeds the combined total for the next three most lethal cancers: breast, colorectal, and prostate.¹ Despite efforts to develop detection technologies and new treatments, little progress has been made to reduce lung cancer mortality over the last 30 years.²

The prognosis for patients with lung cancer is grim. The five-year survival rate is less than 15 percent, a figure that plummets to two percent once the cancer has metastasized.³ In contrast, patients with lung cancer detected at Stage I (localized lesion < 3cm in diameter) have an estimated 88% 10-year survival rate.⁴ Currently, only 16% of lung cancers are detected while still confined to the primary site.⁵

Early detection is essential to the overall improvement of lung cancer outcomes.

The MAC Advantage

In the presence of precancerous lesions, normal cells exhibit subtle changes of their DNA distribution when observed by visible microscopy. These alterations have been designated "Malignancy Associated Changes" (MAC).⁶ By detecting MAC, LungSign™ indicates the presence of cancer in a patient without relying on the occurrence of cancerous cells in the sample.

In the past, MAC assessment required substantial knowledge of the morphological features of chromatin arrangement. With recent advances in digital cell image analysis, MAC has become an effective and practicable predictor of cancer's presence. LungSign™ is the first validated test to be commercialized using this innovative marker for malignancy.

Complementing Current Standards of Care

As the resolution of CT scanners has increased, so has the fraction of patients found to have suspicious nodules. This points to a specificity problem with CT, leading to a high rate of follow-up on false positive results.

In addition, many physicians worry about the effect of CT radiation exposure, especially on population groups for whom radiation should be limited. By updating a patient's pretest risk of lung cancer, LungSign™ may eliminate a significant number of unnecessary CTs.

LungSign™ may also find a role as part of a regular program of testing. Much like Pap testing for cervical cancer, the sensitivity of a single LungSign™ test is expected to improve when applied serially over multiple years as part of a surveillance program.

(1) American Cancer Society. Cancer Facts and Figures, 2006; (2) http://emice.nci.nih.gov/mouse_models/organ_models/lung_models accessed May 2007; (3) Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER 9 Registries for 1988-2002; (4) Henschke CI et al. (2006) Survival of patients with stage I lung cancer detected on CT screening. N Engl J Med 2006;355:1763—1771; (5) <http://seer.cancer.gov/statfacts/html/lungb.html> accessed May 2007; (6) Finch, et al., (1971) Malignancy Associated Changes in Buccal Smears, Acta Cytologica 1971;15: 46-49. and Klawe et al., (1974) Malignancy Associated Changes in Cells of Buccal Smears detected by means of Objective Image Analysis, Acta Cytologica 1974;18: 30-33.



Additionally, there is demand for a means to select individuals for CT lung cancer screening from very high-risk patient groups. LungSign™ provides a good solution, since it is non-invasive, cheap, radiation-free, and the results deliver biologically relevant new information.

Appropriate Patient Groups

Patients for whom LungSign™ is expected to bring benefit include:

- patients suspicious for lung cancer or those being considered for CT screening
- post-CT patients seeking assessment of malignant potential of nodules of undetermined significance
- patients for whom radiation from CT or x-ray should be limited (e.g., women at risk for breast cancer, female smokers, or lung cancer survivors)
- lung cancer survivors monitoring for recurrence
- patients in need of motivation-related smoking cessation tools

Taking the LungSign™ test causes very little physical discomfort. Almost anyone can take the LungSign™ test, with the following exceptions:

- patients who have had thoracic or cardiac surgery within the last 6 months
- patients with asthma or COPD (chronic obstructive lung disease) exacerbation in the last five days
- patients with flu-like symptoms such as fever or chills

Although LungSign™ is a consumer product, orderable by phone and over the Internet, LungSign™ should be requested and interpreted under the care of a physician.

Analysis and Reporting

Once collected, using the LungSign™ sputum collection kit, samples are sent to the Perceptronix Laboratory for analysis. LungSign™ reports are sent to the patient's physician.

Interpreting LungSign™

LungSign™ provides important information about a patient's risk of lung cancer. Likelihood multipliers assigned by LungSign™ update a patient's risk of harboring the disease. Thus, LungSign™ results should be interpreted in the context of a patient's medical history and background risk for lung cancer.

Although not a diagnostic test, the existence of a likelihood predictor such as LungSign™ is potentially of enormous value in the fight against lung cancer.

Perceptronix Medical Inc.

LungSign™ was developed by Perceptronix Medical Inc. Perceptronix believes that early diagnosis is the key to improving outcomes for lung cancer patients. The company, a spin-off of the BC Cancer Agency (Vancouver, Canada), has worked collaboratively with scientists and clinicians from around the world to develop technologies that address the problem of early lung cancer detection.

The goal of Perceptronix is to create products and services that support the early diagnosis of lung cancer for better patient outcomes.

Information and Ordering

toll free: 1.888.629.8779
e-mail: info@LungSign.com
website: www.LungSign.com



About LungSign™¹

LungSign™ is a non-invasive, lung cancer detection test that indicates the likelihood of lung cancer in high risk individuals. It can detect early-stage, pre-symptomatic lung cancer before it is discernable by standard x-ray imaging.

LungSign™ is not meant to be used as a stand alone test for lung cancer. It should be interpreted in conjunction with recognized diagnostic procedures for the management of patients at risk of lung cancer or undergoing post-surgical follow-up. Patients with lung malignancies may have low scores. If a patient has relevant symptoms, further investigation is suggested.

Indications for use

LungSign™ is indicated for the evaluation of patients suspicious for lung cancer due to their:

- Age – Over 50 years old
- Significant smoking history (over 20 pack-years) or exposure to industrial carcinogens
- Symptomology or clinical suspicion of lung cancer

The test has not been validated for patients who have received chemotherapy or radiotherapy and it has not been validated for patients who harbor cancers other than lung cancer.

LungSign™ features:

- Sensitive
- Non-invasive
- Inexpensive
- Patient friendly
- Biologically relevant

How does LungSign™ work?

LungSign™ testing (Figure 1) begins with the collection of a good quality sputum specimen from a patient. Various devices are available to assist patients in the production of such specimens. The specimen is sent to the Perceptronix laboratory where it is analyzed by the LungSign™ automated image cytometer. The result is a single lung cancer likelihood related score derived from the measurements of thousands of cell nuclei.

The unique strength of the LungSign™ Test is that it does not rely upon frankly cancerous cells to indicate that a patient harbours lung cancer.

The LungSign™ Test primarily measures alterations to

normal cells that occur in the presence of a malignancy, a well-documented phenomenon known as Malignancy Associated Changes (“MAC”). This approach sidesteps the problem that cancer cells are seldom present in sputum. Consequently, LungSign™ can assess the likelihood of the presence of cancer from specimens which would not yield useful results via other assays such as conventional cytology or molecular marker based tests.

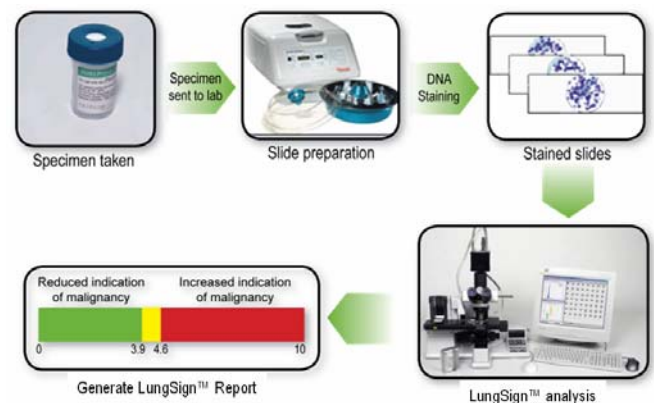


Figure 1. LungSign™ Test process.

What LungSign™ measures

LungSign™ is based on the automated analysis of properties of epithelial cells present in a sputum specimen. The test measures properties of the cell nuclei such as DNA content, conformation and texture. It identifies possible malignant cells (reported independently) as well as changes in normal appearing cell nuclei that are associated with the presence of malignancy (MAC). Available nuclear information is combined into a single score for the specimen.

Ordering LungSign™

LungSign™ should be requested and interpreted under the care of a physician. LungSign™ sample collection kits² are orderable by phone (1-888-629-8779) and over the Internet (www.LungSign.com).

LungSign™ Results

LungSign™ analysis results in a score which is reported to the physician in approximately two weeks.

LungSign™ provides a quantitative measure of cellular abnormality correlated with the presence of lung malignancy. Higher scores suggest an increased likelihood of the presence of lung cancer.



Interpretation Guide

Scores fall into three categories as shown in Table 1.

Table 1. LungSign™ score ranges and corresponding interpretations with regard to likelihood of the presence of malignancy.

LungSign™ Score	Interpretation
<3.9	Decreased likelihood of malignancy
3.9—4.6	Result indeterminate for increased or decreased likelihood of malignancy
>4.6	Increased likelihood of malignancy

These categories are graphically illustrated in Figure 2, where the increase or decrease in the likelihood of the presence of malignancy is shown as a function of score.³

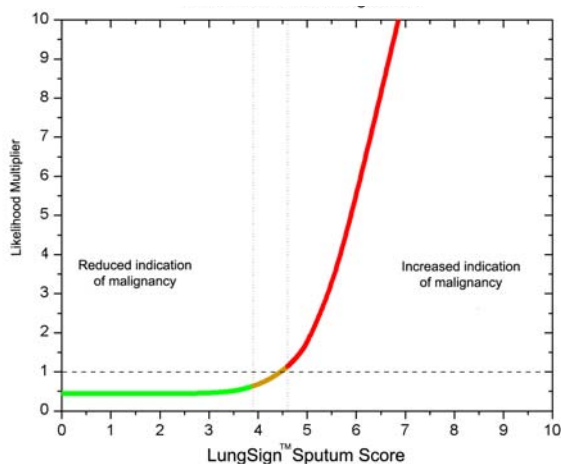


Figure 2. Approximate likelihood ratio multipliers for the odds of harboring lung cancer as a function of LungSign™ score. The red segment represents increased likelihood (scores > 4.6) and the green segment represents decreased likelihood (scores < 3.9), with scores in between (orange) considered indeterminate. For example, with a LungSign™ score of 6 the likelihood that the patient harbors a malignancy is increased by more than 5 times.

The likelihood multiplier updates the patient's post-test risk of lung cancer. It should be interpreted in the context of the relevant lung cancer risk factors and symptoms which specify the patient's pre-test likelihood of harboring the disease.

Pre-test Risk for Screening Population (0.5-2%)

In a screening population consisting of asymptomatic individuals at risk of lung cancer due to age (over 50 years) plus heavy smoking (over 20 pack years) or carcinogen exposure, the disease prevalence may be between 0.5 – 2%.

Pre-test Risk for Very High Risk Population (10%)

The additional presence of symptoms (such as persistent cough or shortness of breath) raise the likelihood of lung cancer and place the patient in a prevalence group that may be 10% or higher.

Table 2 shows estimates⁴ of the LungSign™ predictive values (i.e. the probability of malignancy corresponding to a particular test score) for the 2% and 10% disease-prevalence groups.

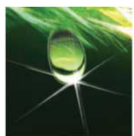
Table 2. Interpretation Guide: Estimates⁴ of the probability of malignancy for LungSign™ scores for different patient populations.

LungSign™ score	Probability of malignancy	
	Screening population (2% prevalence)	Very high risk population (10% prevalence)
1	1	5
2	1	5
3	1	5
3.9	1	7
4	1	7
4.6	2	11
5	3	16
6	10	38
≥7	≥18	≥54

It may be difficult to categorize the patient's pre-test risk, and it is therefore suggested that patients with high scores and those with low scores but suspicious symptomology be referred for further evaluation.

Notes:

- LungSign™ is a test based on ClearSign™ technology. Data presented are quoted from the ClearSign™ clinical trial.
- The performance claims of ClearSign™ were established using induced sputum samples and have not been established for spontaneous product specimens.
- ClearSign™ performance was determined through a blinded clinical trial where the test was prospectively applied to participants who were suspicious for lung cancer. A total of 986 participants with analyzable specimens were included, of whom 330 were determined by conventional means to have lung cancer. The empirically observed performance was 91% specificity and 40% sensitivity for a ClearSign™ score threshold of 5.
- ClearSign™ was studied in a group of patients in the care of lung cancer specialists where the lung cancer prevalence was 33%. The predictive values shown in this table are estimates based on an extension of the test to lower disease-prevalence patient groups and should only be used for general guidance—they are not exact values for either prevalence group.



REQUISITION FORM

Patient Information

Last Name: _____
 Given Names: _____
 Street: _____ Suite: _____
 City: _____ Province/State: _____
 Country: _____ Postal Code: _____
 Tel: _____ Fax: _____
 Email: _____
 Date of Birth: _____ Gender: Male Female
DD-MM-YYYY
 Medical #: _____

Physician Information

Physician: _____ Medical #: _____
 Other Physician: _____ Medical #: _____
 Clinic/Hospital: _____
 Street: _____ Suite: _____
 City: _____ Province/State: _____
 Country: _____ Postal Code: _____
 Tel: _____ Ext: _____ Fax: _____
 Email: _____

Payment Information

Credit Card #: _____ Expiry: _____
MM-YYYY
 Name on Card: _____
 Cardholder Signature: _____
 OR
 Account #: _____

Office Use Only

Paid Cash Debit Credit

Approver Signature: _____

Test Selection

(Select appropriate test and specimen type)

- LungSign™ Test**
- Sputum - Induced (Acoustic)
 - Sputum - Induced (Saline)
- OralAdvance™ Test**
- Buccal Mucosa
 - Other - Specify: _____
- ClearCyte™ Quantitative Cytology**
- Urine - Voided
 - Bladder Washings
 - Urine - Catheterized
 - Pleural Fluid
 - Peritoneal Fluid
 - Fine Needle Aspirate - Site: _____
 - Other - Specify: _____

Collection Information

Date Collected: _____
DD-MM-YYYY

Volume Collected (ml): _____

(Select One)

- Prepared Slide
 Liquid Based

Laboratory Use Only

Date Received: _____
DD-MM-YYYY

Technician Signature: _____

Inspection
 Comments: _____

- Accepted Rejected Pending