

## A Discussion of Lung Cancer & Screening:

### Introduction

Lung cancer is accountable for the death of more individuals than cancers of the breast, colon, cervix and prostate combined. It is the second most common cancer [behind skin cancer] in both men and women and is the most common cause of cancer death in men and women smokers. Lung cancer is usually asymptomatic until it has reached an advanced stage and has one of the poorest prognoses of all cancers with a 5-year survival rate on the order of 15%. The effectiveness of current diagnostic and therapeutic interventions is, however, largely dependent on the “Stage” at which the lung cancer is discovered. Thus, lung cancer is a disease for which screening approaches are very appealing.

Screening is performed to detect disease at a stage when cure or control is potentially possible. It presumes that a test or series of tests will identify asymptomatic persons at risk for the disease. Persons with a positive result on screening can be further evaluated to determine whether they actually have the disease. Ideally, once a diagnosis is determined, early intervention should change the course of the disease, resulting in decreased morbidity and mortality. These basic principles of screening for any disease are very germane to lung cancer. Success however, is based upon several basic assumptions. There must be effective treatment at the preclinical, asymptomatic stage that can reduce mortality in the screened group as compared with the unscreened group. In addition, the sensitivity, specificity, accessibility, cost and associated risks of the screening test itself must be reasonable.

Recent advances in imaging have suggested that low radiation dose computed tomography [CT] has a role in fast, convenient, very safe lung scanning and can diagnose tumors on the order of 5 mm in size. Death from lung cancer is considered preventable in approximately 85% of clinical cases through a combination of avoidance of smoking and early detection.

The following information discusses the concepts of lung cancer, lung cancer detection, screening methods and results.

### Epidemiology of Lung Cancer

Annually, over 160,000 people in the United States die of lung cancer. Cigarette smoking accounts for nearly 90% of all lung cancers. Approximately 30% of the US population is active smokers. The incidence of smoking is similar in men [32%] and women [27%]. The use of cigarettes is directly related to the level of education with 31% being high school graduates, 20% with some college education, and 12% amongst college graduates. However, the overall lifetime risk of developing lung cancer in all smokers is approximately 10%. Passive smoking also contributes to the development of lung cancer among nonsmokers. Certain occupational exposures such as asbestos exposure are also known to cause lung cancer. Air pollution is a probable cause, but makes a relatively small contribution to incidence and mortality. In certain

geographic areas of the US, indoor exposure to radon [found in the soil] may also make a small contribution to the total incidence of lung cancer.

The general public health message has suggested that once people quite smoking, they return to the health profile of a non-smoker; but this is simply not the case. The most important factor is the number of “pack-years” of cigarette use [defined as the number of packs smoked per day times the number of years of smoking]. For instance, a patient who smokes 1 pack per day for 10 years has a total of “10 pack years”. An individual who smokes one-half a pack per day for 20 years also has a 10-pack year equivalent. Even 10 years of moderate smoking can carry some irreversible health risks – including an increased risk of lung cancer. Forty to fifty percent of new lung cancer diagnoses are among former smokers. These may be individuals who smoked from ages 15 to 45, quit, and developed lung cancer at 60. In former smokers who develop lung cancer the time between the diagnosis and abstinence from smoking is 9 years. Over 40 carcinogens [cancer causing materials] have been identified in cigarette smoke. The risk of lung cancer is directly related to the number of cigarettes smoked. The risks for lung cancer can return to the “never-smoked” category, but this is only equivalent after up to 20 years of abstinence.

In the 30-54 year age group, incidence rates among men are double those among women in most racial/ethnic groups. In white non-Hispanics and white Hispanics, however incidence rates for women are closer to those for men. This suggests that smoking cessation and prevention programs may have been especially successful among Caucasian men and/or that such programs have not been as effective among Caucasian women.

Non-small cell carcinoma includes squamous, adenocarcinoma, and large cell carcinoma. This accounts for 85% of all lung cancers. Of these, adenocarcinoma has superseded squamous as the most common type. Although it is not clear as to why the pattern has shifted, the change in consumption from unfiltered high tar cigarettes to filtered low tar cigarettes parallels the change in incidence from squamous cell carcinoma to adenocarcinoma. If detected early, these forms may be amenable to surgical removal.

Small cell carcinoma accounts for the remaining 15% of lung cancers and is characterized by rapid growth and dissemination. Because the disease can spread rapidly [doubling time in volume on the order of 3-6 months] its discovery is often at advanced stages when the cancer may not be amenable to surgical resection. Chemotherapy and radiation therapy are the most common palliative methods employed for small cell carcinoma.

Each year approximately 193,000 new cases of lung cancer are reported in the US [112,200 in men and 81,700 in women]. The 1-year relative survival rate for lung cancer has risen from 32% in 1973 to 41% in the 1990's. However, the combined 5-year relative survival rate for all lung cancer stages remains between 13-15% [i.e. a roughly 85% mortality]. Although the 5-year survival rate is 47% for cases detected when the disease is at an early, localized stage, only approximately 15% of malignant lesions are currently identified at this stage of the disease.

### **Lung Cancer Staging**

The staging of lung cancer is very important in clinical decision making. The current staging system for non-small cell lung cancer was adopted in 1997. The four stages of lung cancer are based upon the TNM descriptors. T stands for Primary Tumor Size or Extent; N stands for

Regional Lymph Node Involvement; M stands for Absence or Presence of Distant Metastasis. The most pertinent of these divisions, as it pertains to imaging/screening for lung cancer are: T0 – no evidence for a primary tumor; T1 – tumor  $\leq$  3 cm in greatest dimension and no invasion of bronchi; T2 -  $>$  3 cm in size or involves bronchus, visceral pleura, or regional telecasts; T3 – tumor of any size with invasion of chest wall, diaphragm, mediastinum; T4 – tumor of any size that invades heart, great vessels, trachea, esophagus, vertebral body, or with malignant effusion. N0 – no regional lymph node metastasis; N1 – metastasis to lymph nodes on the same side of the chest as the tumor; N2 – metastasis to mediastinal lymph nodes or distant lymph nodes. M0 – no distant metastasis; M1 – distant metastasis present.

Based upon the above, lung cancer is divided into Stages (I, II, III, IV) according to the following table:

Stage	TMN Subset
IA	T1 N0 M0
IB	T2 N0 M0
IIA	T1 N1 M0
IIB	T2 N1 M0, T3 N0 M0
IIIA	T3 N1 M0, T1 N2 M0 T2 N2 M0, T3 N2 M0
IIIB	T4 N0 M0, T4 N1 M0 T4 N2 M0, T1 N3 M0
IV	T2 N3 M0, T3 N3 M0, T4 N3 M0 Any T Any N M1

Approximately 50% of patients survive five years if the disease is diagnosed while still localized. In patients with Stage I disease, survival is better among patients with T1 tumors compared with T2 tumors. Survival appears to be further improved among patients with smaller T1 lesions. It has been observed that significantly better survival can be seen among those with T1 lesions smaller than 10 mm compared with individuals with larger T1 lesions and data show progressively better five-year survival among patients with smaller T1 lesions. In contrast, one study observed no survival advantage by tumor size among 500 patients with tumors smaller than 30 mm. However, there are little to no data for tumors in the range of  $>$ 10 mm and  $<$ 20 mm in size. Nevertheless, only 16% of new diagnoses made by chest x-ray or from sputum examination are classified at the localized stage and fewer than 25% of patients on average who present with lung cancer are asymptomatic at the time of diagnosis.

The complex TNM system is not used for small cell carcinoma and is replaced by a simple two-stage system of either limited or extensive disease. Limited disease is defined as disease confined to one side of the chest with or without local lymph node involvement while extensive disease defines a person with disease outside the defined area.

### Lung Cancer Detection [Screening] Technology

There are several methods of “screening” for lung cancer that have been used in some studies or are in the process of being used in developing studies.

a. Chest X-ray

Chest x-ray is simple, fast, and widely available. Normally two images are taken – a posterior/anterior view and a lateral view. The total radiation to the patient is small. The sensitivity of chest x-ray for lung cancer detection is dependent on the size and location of the

lesion, quality assurance factors related to image quality, and the skill of the interpreting physician. Studies have demonstrated that conventional chest x-ray has a sensitivity of only about 16% in detecting Stage I disease. Failure to detect lesions at a favorable size, or even larger, can occur because the mediastinum and other aspects of chest structure may obstruct the view. Errors in perception on the part of the interpreter are also common.

b. Sputum Cytology

Tumors that have invaded into the bronchus can result in some of these “neoplastic” cells entering into the normal production of sputum. However, the collection must be done in a proper fashion such that the cells from the deeper portions of the bronchial tree are sampled. Multiple samples may be necessary. The pathology laboratory must also be prepared to handle the specimens properly. In some trials, approximately one in four squamous cell cancers were detected by sputum cytology at a favorable stage. Although brushings and washings of bronchial membranes by bronchoscopy provide a better yield, bronchoscopy is mildly invasive. One disadvantage of sputum cytology is that other methods must be applied to identify the location of the cancer.

c. Molecular Screening

This is a developing method for early detection of lung cancer that includes fluorescence bronchoscopy and molecular screening for mutations associated with transformation of bronchial epithelial cells into cells that are potentially malignant. Evaluation of lung epithelium for evidence of accumulated genetic damage through polymerase chain reaction [PCR] techniques is another new area of investigation. Although malignant lesions have been found, the sensitivity and specificity of this for more peripheral lesions remain suboptimal.

d. Low Radiation Dose Computed Tomography

X-ray computed tomography examination of the chest and lungs is an established method. Generally the older CT scanners were unable to acquire images of the entire chest in a single breathhold and produced moderately high radiation doses. Both of these limitations attenuated any initial enthusiasm for using CT as a screening tool for lung cancer.

The development of a newer generation of “helical” [or “spiral”] CT scanners has brought this issue back to the forefront. Electron Beam Tomography [EBT] offers a unique scanning architecture that allows complete chest imaging somewhat faster, but in a manner comparable to the latest generation of “high resolution” helical CT devices. Radiation doses can be adjusted for helical devices performing chest CT yielding amounts roughly on the order of 5-10 chest x-rays. EBT chest imaging affords even a lower radiation dose than that of helical CT, but offers the advantage of maintaining the “high resolution” details of the scan.

Using thin slice tomography, the helical CT devices can image the entire lung and define the site of lung nodules roughly on the order of 5 mm. EBT, using specialized protocols, can potentially define nodules of even smaller size, with no increase in radiation dose, using 3-D imaging methods.

### **Prior Trials for Lung Cancer “Screening”**

Beginning in the 1950’s there were several nonrandomized, uncontrolled screening studies performed. One study enrolled approximately 20,000 patients but showed no benefit to survival after a screening chest x-ray. On the other hand, at this time, there was little other than palliative care for patients with advanced lung cancer. Other studies were done in Tokyo, London and Germany between 1959 and 1972 and consisted of chest x-ray surveys. These suggested that

there was some improvement in survival, but mortality from lung cancer could not be adequately measured or was not improved in screened subjects as compared to control groups.

In the early 1970's, four randomized, controlled trials were set up using chest radiography and sputum cytology. These were the Johns Hopkins Lung Project, the Memorial Sloan-Kettering Lung Project, the Mayo Lung Project, and a study done in Czechoslovakia. The total enrollment was on the order of 37,000 patients.

Analysis of these trials produced some expected and some unexpected results. There was an increased incidence of earlier stage lung cancers, more cancers cured by surgery, and improved five-year survival rates in the screened groups compared with the control groups [35% vs. 15%]. However, there was no statistically significant difference in total mortality attributable to lung cancer between the two groups. In other words, patients with lung cancer in the screened groups had a higher likelihood of undergoing surgical resection and lived longer than those in the control groups, but equal numbers of patients in both groups ultimately died from their disease.

However, one must also look more closely at the data. In the Johns Hopkins Lung Project, 50% of the patients in whom lung cancer developed had negative findings at the time of screening and manifested symptoms before the next scheduled follow-up. Although this could suggest that this was attributable to more aggressive tumors, this does not fit the general biological model of lung cancers. An alternative is that the screening method was not that sensitive. Missed tumors by a screening method does not mean that screening does not work, but that the method used was of little benefit over not doing screening in the first place. In addition some of the patients with small primary lesions already had distant metastases that were not detected by chest x-ray or cytology. Finally, the supposition is that the screened patients would have less advanced disease at the time of discovery compared to the control subjects. Although there were more early disease cases found in the screened group, the number of patients with advanced stage disease was not lower in the screened group compared to the control group. Since advanced lung cancer found incidentally or found at the time of a screening chest x-ray would likely not have a difference in survival, the conclusion that screening in patients with early disease would not be beneficial cannot be made from these results.

The Mayo Lung Project enrolled more than 10,000 male smokers between 1971 and 1976. This study examined whether frequent surveillance chest x-rays and sputum tests would save lives from lung cancer. Examining how many men in the screened group died of lung cancer compared to the routine care group they found no significant difference in the number who died from lung cancer in either set of patients. Although the screening done during this 6 year period did not apparently save lives, it did find more lung cancers. Additionally, the cancer patients in the screened group lived longer than the cancer patients in the routine care group. The Mayo researchers explained this apparent paradox by suggesting that some of the cancers found in men in the screened group would not have killed them, indicating that these lung cancers were probably growing very slowly or may not have grown at all. Again, however the method of screening used [chest x-ray and sputum cytology] has only a moderate sensitivity and specificity for detecting lung cancers at any stage. Additionally, these patients were all smokers and had additionally a significant occurrence of other smoking related lung diseases as well as a higher risk for death from heart disease than the general population.

In summary, prospective studies of lung cancer screening using chest x-ray and/or sputum cytology have not demonstrated persuasively that screening for lung cancer with chest radiography alone or in combination with sputum cytology saves lives. While the results of prospective trials have been disappointing, especially in view of the overall burden of this disease, these trials also were methodologically limited at inception in their ability to demonstrate a benefit from screening. Although none of the studies showed fewer deaths in the experimental group compared with the control group, none of the studies compared disease outcome in a group offered screening with a group strictly not invited to or encouraged to have screening. However, given the current issues of screening for preventable diseases the pure conduct of such a “proper” trial is unlikely as well as not practical.

### **Low Radiation Dose Computed Tomography for Screening**

The results of the trials noted above have been questioned and criticized. Concerns regarding study design, statistical analysis, contamination, interpretation bias [real and perceived], and limited sensitivity of the technology have suggested that newer forms of diagnostic imaging may provide more superior results. As commented upon above, low radiation dose CT offers a opportunity to visualize the entire chest and facilitate identification of nodules or tumors, make direct digital measures of size, examination of central and peripheral lymph nodes, define the potential for development of local as well as distant metastases, as well as examine the pleura, pericardium, trachea, and bronchial tree. In addition 3-D visualization techniques can define imaging planes from virtually any conceivable angle or of any slice thickness.

Two non-randomized studies from Japan have been published using low dose CT, chest x-ray, and three-day pooled sputum samples. An additional study, the Early Lung Cancer Action Project [ELCAP] has been published examining in a non-randomized protocol, the use of chest x-ray and low dose CT chest imaging.

In the Japanese studies the number of lung cancers detected when CT was added to the screening program [chest x-ray/sputum] nearly tripled (2.6 fold increase). In addition the proportion of Stage I lesions increased from 53% to 93% and the mean diameter of detected tumors decreased from 30 mm to 12 mm in size. CT detected all lesions found on chest x-ray. Only 3 of 18 tumors were detected by sputum cytology alone.

ELCAP beginning in 1992 enrolled 1,000 volunteers aged 60 years and older with at least a 10 pack year history of smoking and who would be acceptable candidates for thoracic surgery. The baseline prevalence/screening experience was published in The Lancet in 1999. Low dose CT identified 233 participants with non-calcified nodules and 27 malignancies, 26 of which were resectable and 23 of which represented Stage I disease. In contrast, chest x-ray identified 68 non-calcified nodules, 7 of which were malignant. Work up of positive CT results was based on the initial size of the nodule and any changes on repeat screening.

The results of the initial Japanese and ELCAP publications can be summarized as follows:

- By low dose CT, nodules were detected three times as commonly as on chest x-ray
- Detection of malignant tumors were four times as common as that detected by conventional chest imaging
- Detection of Stage I malignant tumors were six times as common.

- Malignant tumors detected on low dose CT were substantially smaller than those detected on chest x-ray

The conclusions of these studies was that low dose CT can greatly improve the likelihood of detection of early lung cancers, and thus potentially at the more curable stage.

### **The Controversy**

Critics of screening have agreed that it facilitates detection of lung cancer earlier than in control groups but point out that screening does not clearly save lives. They suggest that although survival from the time of diagnosis of the disease is commonly reported in screening trials, it is not an appropriate measure of a diagnostic screening test and can be misleading because it is subject to “lead-time bias”, “length-time bias”, and “overdiagnosis bias”. These issues are tempered by influences of “pseudodisease diagnosis” and “sticking diagnosis bias”.

The issue of “pseudodisease” is that some of the tumors found may have a naturally more benign clinical course and the patient may die from another problem such as emphysema or heart disease before he/she may have died from the lung cancer. “Sticking diagnosis bias” enters when a patient in a study was diagnosed with the label “lung cancer” and then subsequently dies. Doctors are more likely to list lung cancer as the cause of death, even when it was not proven by autopsy. In other words, some of the study participants whose records show lung cancer as their cause of death may have actually died of other causes. This actually biases the study’s results against the case for screening.

For lead-time bias, the diagnosis of disease is made earlier in the screened group, resulting in an apparent increase in survival time, although the actual time of death may be the same for both screened and control groups. However, this belies the issue of developing an effective treatment program for those with an early diagnosis through screening. Although it is likely true that incidental findings of asymptomatic but advanced tumors may not reduce eventual mortality, data consistently demonstrate that initial tumor size [although not ruling out the potential for distant metastasis] is a very important determinant in a cure.

To understand length-time bias it must be understood that the probability of detecting disease is related to the growth rate of the tumor and how this might fit into the timing of an incidental “screening” procedure. Aggressive, rapidly growing tumors have a short potential screening period [the interval between possible detection and the occurrence of symptoms]. Thus, unless the screening test is repeated frequently, patients with aggressive tumors are more likely to present with symptoms. More slowly growing tumors have a longer potential screening portal and are more likely to be detected when the patient is asymptomatic. As a result, a higher proportion of indolent [slow growing] tumors is found in the screened group, causing an apparent improvement in survival. However, this interpretation needs to be evaluated in the context of the screening test performed. As noted above 50% of the patients in whom lung cancer developed in the Johns Hopkins Lung Project had negative findings at the time of chest x-ray screening and manifested symptoms before the next scheduled follow up. On the surface this might suggest that the follow up period was too long, but it may also have been because of the accuracy of the screening. Chest x-ray is limited by the capabilities of the technology and observer variation among radiologists. Suboptimal technique, insufficient exposure, and poor positioning and cooperation of the patient can obscure pulmonary nodules or introduce artifacts. Furthermore, there is wide intraobserver variability [up to 40%] with chest x-ray. Most errors

are false-negative interpretations, and pulmonary and hilar masses are among the most commonly missed diagnoses.

Overdiagnosis bias is an extreme form of length-time bias. The detection of very slow growing tumors in a screened population produces an apparent increase in the number of cases of lung cancer and an apparent increase in survival for patients found by screening. However, perhaps only a portion of the patients [screened or controls] will die from the slow growing lung cancer, but most may die of other unrelated causes. This overlaps with the “sticking diagnosis bias” in which the patient found to have lung cancer by screening may have his/her death attributed to “cancer” where the others that were not diagnosed may have their deaths attributed to “natural causes”.

Most of the controversy about screening for lung cancer is related to interpretation of older studies using technology that was not particularly sensitive in detecting tumors. Additionally, the trials were not necessarily designed to detect differences in mortality. As a result, looking at these trials for guidance is not overly useful.

However, many of the issues related to this controversy are not necessarily because of the screening technology, but the lack of proper medical program to be in place AFTER the patient has the screening test and is found to have an abnormality. A patient found to have or be suspected of lung cancer following a screening test might avoid or be opposed to any proper medical intervention. This has a myriad of causes and should not reflect on the screening method, but the ineffective follow-up of the screened patient. Thus the key to success is to develop a proper program to document the stage of the cancer, to document growth to avoid unnecessary additional tests that do not need to be done, and to document a program of repeat testing. To accomplish this, any program needs to have proper support personnel in place that involves not only radiologists reviewing the images, but pulmonary disease specialists and thoracic surgeons. Furthermore, the clinical program must be conducted always with the best interests of the patient in mind and a plan of close follow-up in cases found to have abnormal tests.

The American Cancer Society [ACS], long considered to be opposed to broad based screening programs, has recently taken another view of lung cancer screening, especially in the context of using low radiation dose CT lung scanning. They currently continue to NOT endorse widespread “screening” and discourage testing in a setting that is not linked to multi-disciplinary specialty groups for diagnosis and follow-up. Furthermore, individuals who choose to undergo testing should have access to testing and follow-up that meets state-of-the-art standards, with informed decision-making at every step of an ongoing process. However, a widespread screening program and assessment of a given individual “at risk” are not the same. In contrast, the ACS does NOT discourage individual patient assessment. The ACS does recommend that referral of the patient is most proper from their primary care physician who would have prepared the individual to understand the risks and to have jointly reached informed decisions about testing. However, in a recent discussion on ACS guidelines for Early Detection of Cancer (CA Cancer J Clin 2001;51:38-75), it is stated: “Absence of a referral from a primary care physician due to lack of provider endorsement of testing, or not having a primary care provider, should not be a barrier to testing. However, if an individual seeks testing and does not have a referral from a primary care provided, the [physician] who provides testing is obliged to provide information

about benefits, risks and limitations of testing as described ..., and must become the individual's physician of record until proper alternative care arrangements can be made.”

The goals of any program must then be consonant with excellence in clinical practice and this involves identification of the appropriate patient for screening; use of the best available method for screening; and development of a program in place to determine what to do with the patients after the test is done. The program must act in a responsible manner towards these goals; this involves a composite of information and the cooperation of radiologists, internists, family practice doctors, pulmonary disease specialists and thoracic surgeons

### **Identification of Patients for Lung Screening**

Patients appropriate for lung cancer screening are individuals that are “at risk” for lung cancer. Based upon the general understanding of the causes of lung cancer, the following represents a listing of such individuals:

- Individuals of any age with at least a 10 pack year history of cigarette use
- Former smokers with at least 10 pack year history who have quit <15 years prior
- Workers in an occupation where there is exposure to air pollutants/dust or asbestos
- Non-smokers who live with active smokers
- Individuals who have a family history of lung cancer
- Individuals experiencing symptoms such as persistent phlegm, chronic productive and non-productive cough, blood in sputum, or progressive shortness of breath
- Individuals who have a significant exposure to radon

**Recommendations for Evaluation/Follow up in Patients Identified by CT:** Although decisions about further testing and possible biopsy are at the discretion of the patient's personal physician, certain recommendations can be initially made regarding the results of the EBT/CT scan. The following relates to the finding of a single or multiple pulmonary nodules. Additional findings on the lung scan which are not felt to directly impact on the potential for lung cancer are included in the Radiologist's report and directed to the patient's primary care/referring physician or sent back to the patient with additional commentary where appropriate. For situations involving pulmonary nodules, the patient's primary care physician is advised of the results. The protocol for pulmonary nodules, which is similar to that employed by ELCAP, is as follows:

If old films are available, they should be reviewed to determine whether the findings on the CT scan represent a new finding. Generally, if a nodule shows no growth over 2 years, it can be considered benign. If old films are not available or are inconclusive and between one and six non-calcified nodules are identified on the high resolution EBT, a standard-dose high resolution CT scan of the chest with intravenous contrast injection to determine if there is vascular opacification of the nodules(s) is recommended. If the contrast high-resolution CT shows benign calcification not identified on the EBT/CT scan, in terms of extent or distribution, in a nodule with smooth edges and size less than 20 mm, the nodule can usually be classified as benign. If these criteria are not met by all of the non-calcified nodules, further investigation is recommended as follows.

- $\leq 5$  mm in size: follow up by EBT/CT or conventional high resolution CT 3 months later, and if there is no growth, repeat CT scanning at 6 months, 12 months, and 24 months.

- 6-10 mm in size: each nodule should be assessed on an individual basis for the possibility of undertaking a percutaneous needle biopsy or surgical biopsy. If the risk of biopsy is inappropriately high, follow-up for growth, as described above, is recommended.
- $\geq 11$  mm in size: biopsy recommended.

If the EBT/CT scan demonstrates finding highly consistent with lung cancer, such as a mass, apparent “mass affect”, suspicious lymphadenopathy, question of pleural involvement, or obstructive pneumonia, then personal contact with the patient’s primary care physician is needed.

If the initial or baseline EBC is negative for nodules, follow-up yearly scan may be indicated, depending on the patient's risk for the development of lung cancer.

### Summary

At the present time, the early detection of lung cancer and precursor lesions offers a largely unmet potential to reduce morbidity and mortality from malignancies. Presently, screening in the US is “opportunistic” [rather than being performed on a regular basis], and thus the absence of a systematic approach to screening and follow-up means a high proportion of incident cases that may have less than optimal prognosis. There remains considerable need for improvement over “screening without conscience” and thus considerable opportunity to offer a proper screening program that makes sense clinically to the patient and to their doctor.



Medical Director,  
PrevaHealth Wellness Diagnostic Center

### Bibliography:

Patz EF, Goodman PC, Bepler G: Screening for Lung Cancer. *New Engl J of Med* 2000; 343:1627-1633

Shusuke S, Takashima S, Li F, et al: Mass screening for lung cancer with mobile spiral computed tomography scanner. *Lancet* 198;351:1243-45

Miettinen OS, Henschke CI. CT screening for lung cancer: coping with Nihilistic Recommendations. *Radiology* 2001;221:592-596

Henschke CI, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. *Lancet* 1999;354:99-105

Yankelevitz DF, Reeves AP, Kostis WJ, Zhao B, Henschke CI. Small pulmonary nodules: volumetrically determined growth rates bases on CT evaluation. *Radiology* 2000;217:251-256

Diederich S, Wormanns D, Heindel W. Lung cancer screening with low-dose CT. *European Journal of Radiology* 2003;45:2-7