



MedStar Health
Cancer Network

November 17, 2017

A Chronology of Advancements in the Diagnosing of Lung Nodules

Presenter: Daniel P. Harley, MD, MSB, FACS
Surgical Director of the Angelos Center for Lung Diseases



Pulmonary Nodules

- Small radiographic nodules that may be solitary or multiple
- Somewhat spherical, well circumscribed and less than or equal to 30 mm in diameter and are completely surrounded by aerated lung.
- Adjectives to describe the nodules could include:
 - Spiculated
 - Dense
 - Mixed density
 - Ground glass



Implications

- The widespread use of various types of chest imaging has led to finding a virtual myriad of pulmonary nodules worldwide.
- The goal and the dilemma for clinicians is to distinguish between benign and malignant nodules and
- Minimize the testing of those that are ultimately proven to be benign

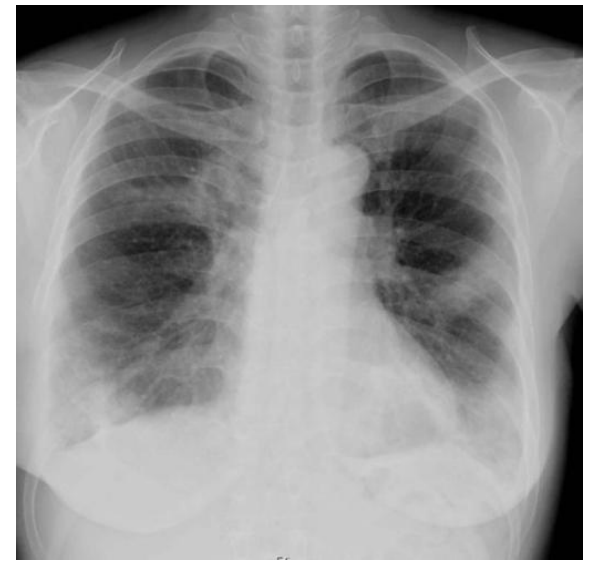


Philosophy

- George Santayana—Harvard philosopher posited:
 - “Those who do not remember history are bound to repeat it.”
- William of Occam, an Oxford philosopher (c. 1100) who posited:
 - “Entia non sunt multiplicanda prater necessitatum”



Chest Roentgenograms

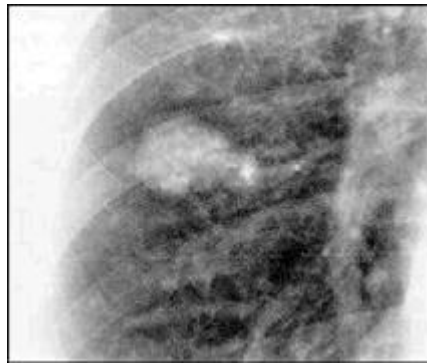


- Before chest roentgenograms, the only pulmonary nodules that were recognized were those found at autopsy.
- Chest roentgenography was introduced in 1896 and overnight pulmonary nodules became a common finding.
- A Clinical conundrum had been introduced:
 - What were they?
 - How would they be diagnosed with minimal intervention?

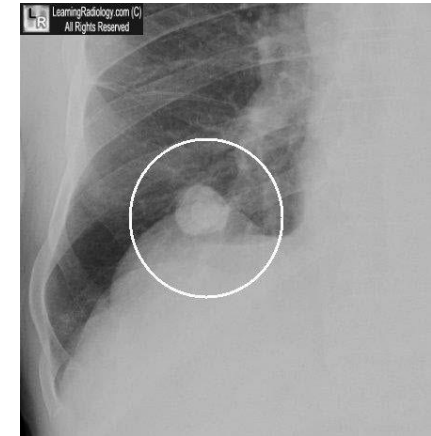


Benign

- Hamartoma
- Granuloma
- Aspergilloma
- Coccidiomycoma
- Cryptococcus
- Histoplasmosis
- Tuberculoma
- Hemangioma
- AVM
- Bronchogenic cyst
- Rounded Atelectasis



Hamartoma

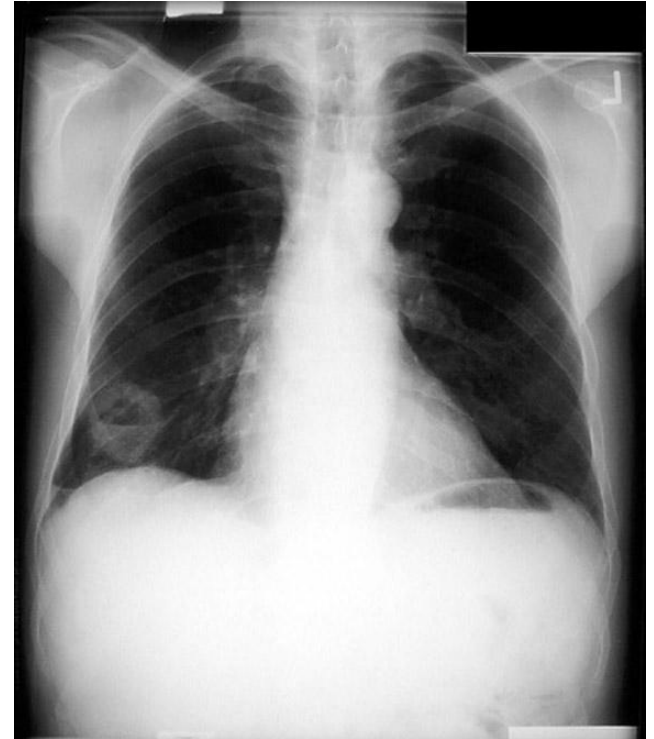


Histoplasmosis



Malignant

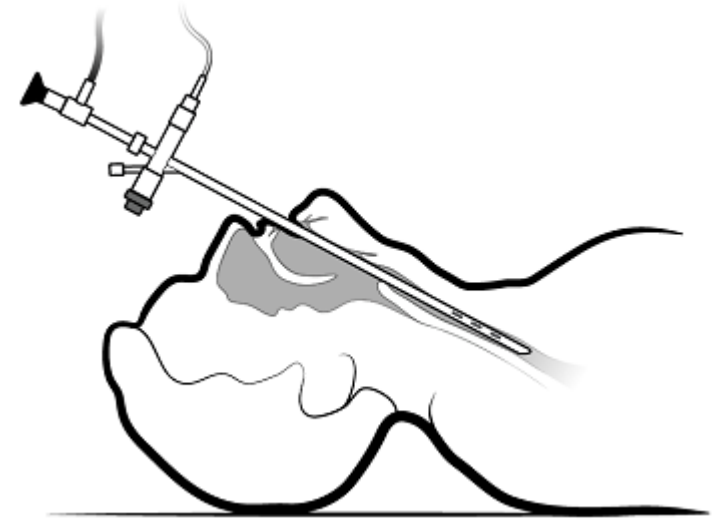
- Adenocarcinoma
- Squamous Cell carcinoma
- Large Cell carcinoma
- Carcinoid tumor
- Metastatic carcinoma
- Small Cell cancer





Bronchoscopy

- At about the same time as the introduction of Roentgenography, the rigid bronchoscope was developed.
- Access to the tracheas and main stem bronchi was good, but access to the lobar and segmental bronchi was poor
 - Visualization was like looking down the barrel of a ball point pen
- Overall diagnostic yield was and is poor.





State of the Art: 1964

- John Steele, MD published a monograph: “The Solitary Pulmonary Nodule”
- He analyzed a total of 1,034 pulmonary nodules
 - 887 males underwent resection
 - 316 of these resections revealed a malignancy
 - 65.5 % of the resections revealed benign disease.
- Those results would be unacceptable and deplorable today!



Improvements

- Geoffrey Hounsfield of EMI Laboratories and Alan Comack of Tufts University developed computed tomographic imaging—CT in 1974
 - Subsequently won a Nobel Prize
- CT became universally used in the ensuing decades

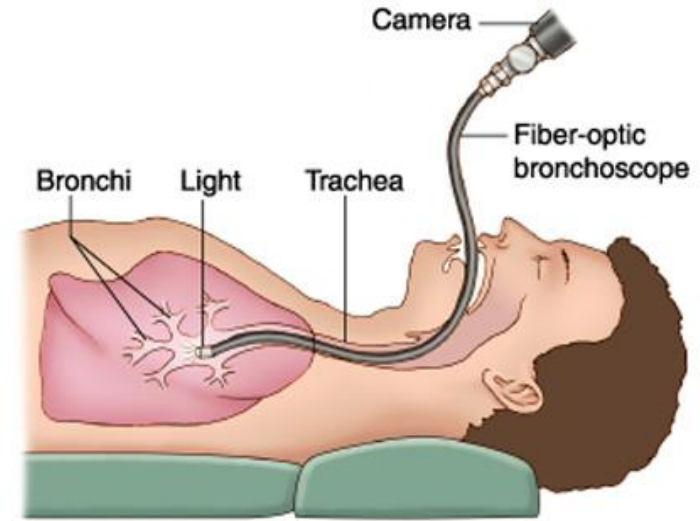


Improvements

- CT images gave increased information about a pulmonary nodule's morphology and consistency.
- Modifications allowed for fine needle aspirate biopsies of nodules that were relatively peripheral in location.

Continued Improvements

- Shigedo Ikeda developed the fiberoptic bronchoscopy in 1964
- Potentially it allowed access to modules in all areas of the lung.
- The addition of the Endobronchial ultrasound (EBUS) and Electromagnetic Bronchoscopy during the last 2 decades made access to all areas of the lung a reality.





Continued Improvements

- Positron emission tomographic scans (PET)
- For the diagnosis of lung cancer,
 - Overall sensitivity of 96%
 - A specificity of 79%
 - Accuracy of 91%



The Dilemma Revisited

- Despite all of the improved technology, all the marvelous diagnostic tests, there is no simple or multiplicity of simple tests able to accurately diagnose the etiology of a single or multiple pulmonary nodules.
- Most of the tests are expensive and invasive and often the diagnosis is still made by deduction.
- Worse yet, only 20% of biopsied pulmonary nodules demonstrate malignancy.



What is needed?

- A simple test that is accurate, easy to administer, readily available and inexpensive.



Possibilities – Liquid biopsies

- Multiple platforms are currently being investigated
- Many involve a 13-protein panel
- They allow for the isolation and identification of CT DNA, exosomes, tumor educated platelets and CTCs.
- These tests currently identify benign nodules with 94% accuracy.



Possibilities: Breath biopsies

- Dogs can recognize lung and breath cancer in the exhalations of patients with those cancers.
- Dogs have a detection threshold of several parts per trillion.





What are they smelling?

- Volatile Organic Compounds (VOCs)
- There is not one diagnostic VOC, but a combination of more than one VOC may be diagnostic.
- VOCs are analyzed by gas chromatography and mass spectrometry.
- They can be diagnostic of lung cancer, COPD, asthma and cystic fibrosis.



The Future

- Liquid biopsies and Breath biopsies may be the future in the diagnosis of lung nodules





The Future

- What about this “*entia non sunt multiplicanda praeter necessitatum*”?
 - This means: single entities should not be multiplied needlessly.
- In terms of lung nodules, their diagnosis should be made simply, accurately , and with a minimum of fuss and expense.