# NSCLC PERSONALIZED MEDICINE VIA INTEGRATION INTO BIO-MATHEMATICAL MODEL INDIVIDUAL CLINICAL DATA AND PROGNOSTIC/PREDICTIVE BIOMARKERS.

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# Background

- Lung cancer is the most common cause of cancer death in the US and worldwide.
- 215.000 Americans have died of lung cancer in 2008.
- 1 in 7 smokers will die of lung cancer.
- The avarage 5 year survival- 15%.

# BACKGROUND

## FIGURE 1 Ten Leading Cancer Types for Estimated New Cancer Cases and Deaths, by Sex, United States, 2009

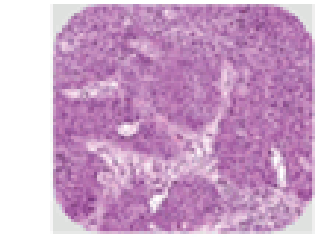
Estimated New Cases*

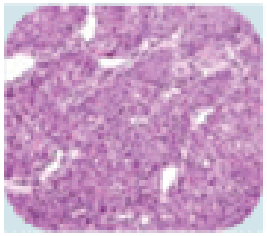
| Males | | | | Females | | |
|---|---|---|---|---|---|---|
| Prostate | 192,280 | 25% | | Breast | 192,370 | 27% |
| Lung & bronchus | 116,090 | 15% | | Lung & bronchus | 103,350 | 14% |
| Colon & rectum | 75,590 | 10% | | Colon & rectum | 71,380 | 10% |
| Urinary bladder | 52,810 | 7% | | Uterine corpus | 42,160 | 6% |
| Melanoma of the skin | 39,080 | 5% | | Non-Hodgkin lymphoma | 29,990 | 4% |
| Non-Hodgkin lymphoma | 35,990 | 5% | | Melanoma of the skin | 29,640 | 4% |
| Kidney & renal pelvis | 35,430 | 5% | | Thyroid | 27,200 | 4% |
| Leukemia | 25,630 | 3% | | Kidney & renal pelvis | 22,330 | 3% |
| Oral cavity & pharynx | 25,240 | 3% | | Ovary | 21,550 | 3% |
| Pancreas | 21,050 | 3% | | Pancreas | 21,420 | 3% |
| **All Sites** | **766,130** | **100%** | | **All Sites** | **713,220** | **100%** |

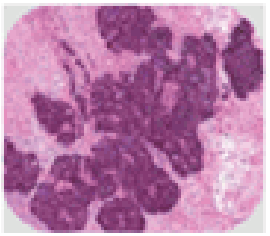
Estimated Deaths

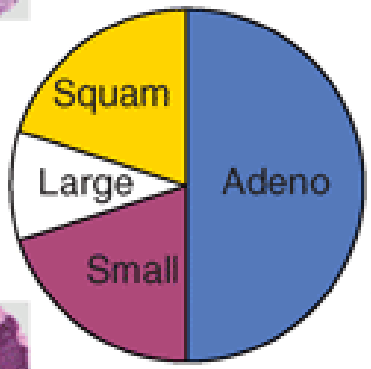
| Males | | | | Females | | |
|---|---|---|---|---|---|---|
| Lung & bronchus | 88,900 | 30% | | Lung & bronchus | 70,490 | 26% |
| Prostate | 27,360 | 9% | | Breast | 40,170 | 15% |
| Colon & rectum | 25,240 | 9% | | Colon & rectum | 24,680 | 9% |
| Pancreas | 18,030 | 6% | | Pancreas | 17,210 | 6% |
| Leukemia | 12,590 | 4% | | Ovary | 14,600 | 5% |
| Liver & intrahepatic bile duct | 12,090 | 4% | | Non-Hodgkin lymphoma | 9,670 | 4% |
| Esophagus | 11,490 | 4% | | Leukemia | 9,280 | 3% |
| Urinary bladder | 10,180 | 3% | | Uterine Corpus | 7,780 | 3% |
| Non-Hodgkin lymphoma | 9,830 | 3% | | Liver & intrahepatic bile duct | 6,070 | 2% |
| Kidney & renal pelvis | 8,160 | 3% | | Brain & other nervous system | 5,590 | 2% |
| **All Sites** | **292,540** | **100%** | | **All Sites** | **269,800** | **100%** |

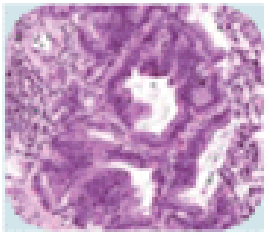
# Histologic Classification









Small Cell Lung Cancer (SCLC)

Non-Small Cell Lung Cancer (NSCLC):
- Adenocarcinoma
- Squamous cell carcinoma
- Large cell carcinoma

Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

# How can we diagnose ?

# DIAGNOSTING TOOLS

- Symptomes – not specific !
  Cough, weight loss, dyspnea, hemoptysis, clubbing.

- Chest Radiograph

- PET-CT

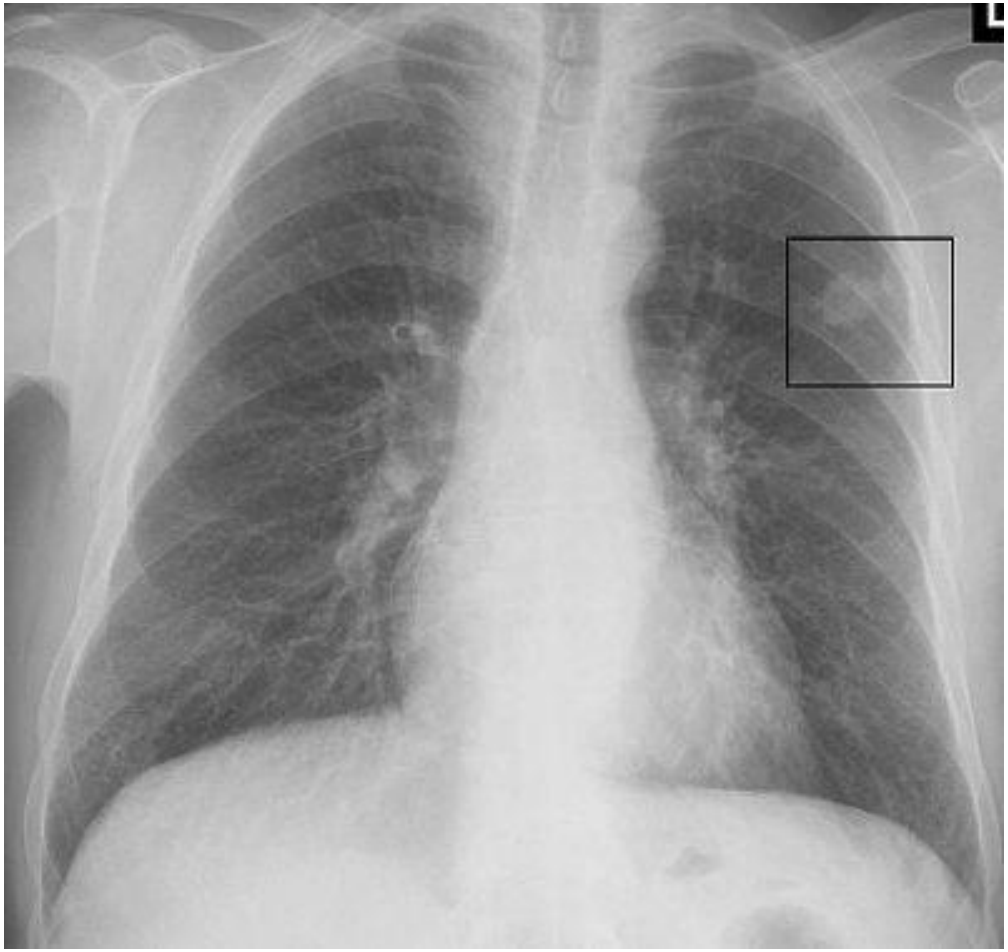
- CT

- Bronchoscopy

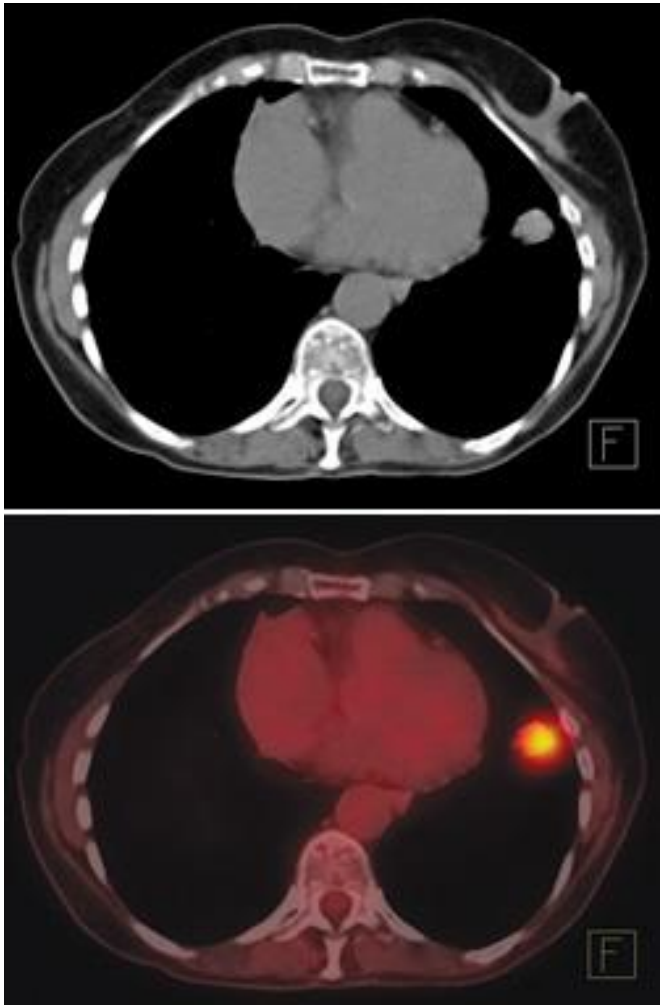
# Clubbing

# Chest Radiograph

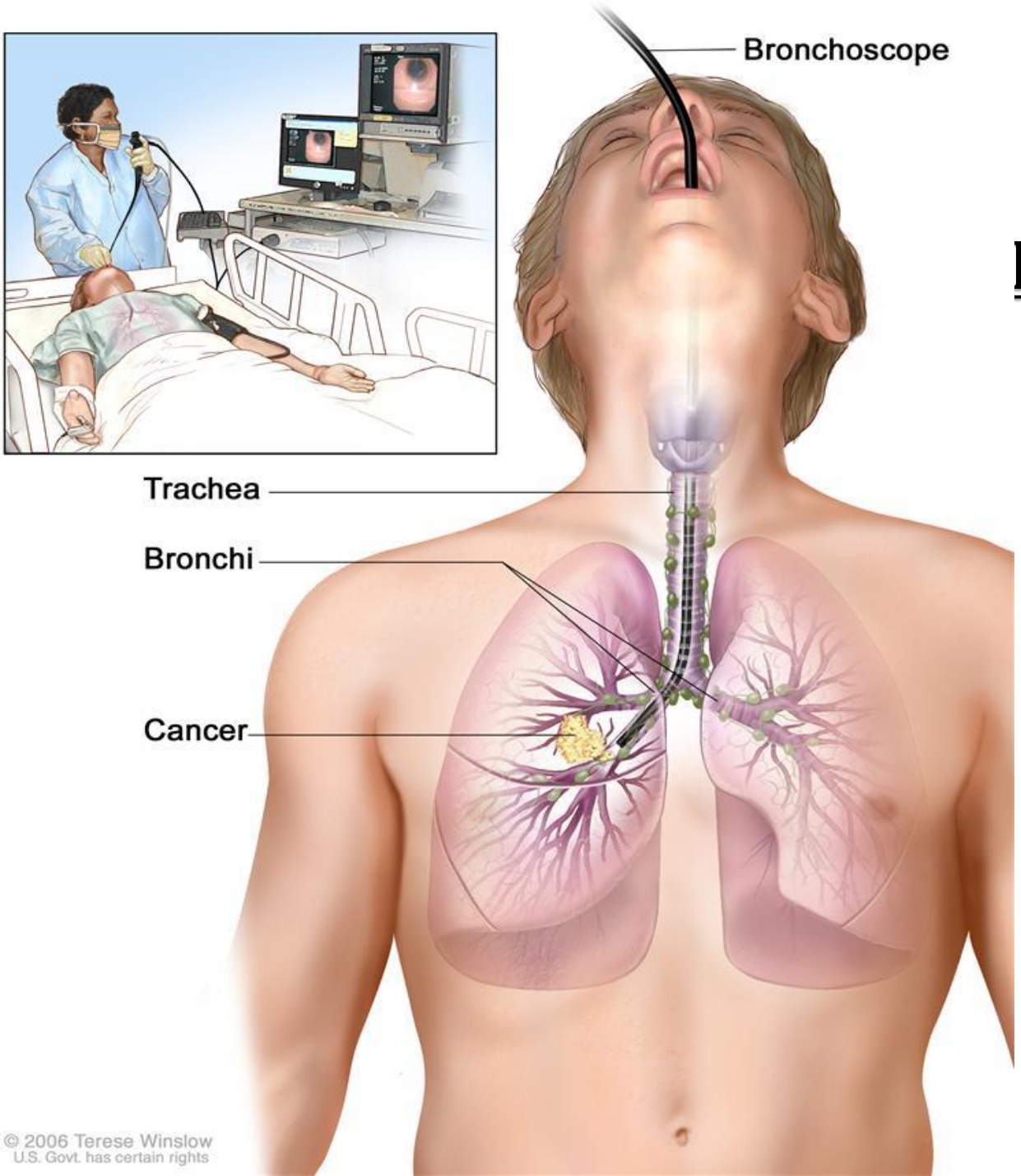
# Chest Radiograph



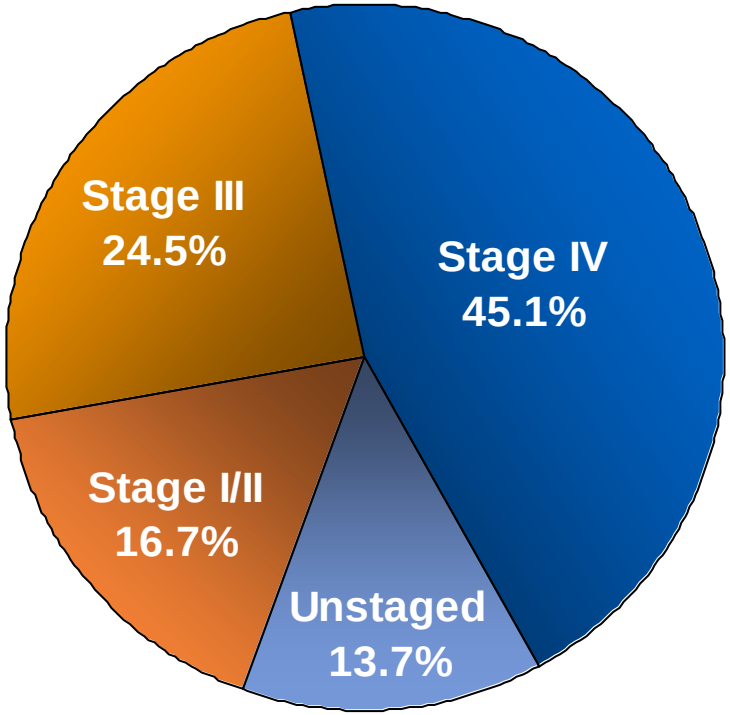
# PET CT



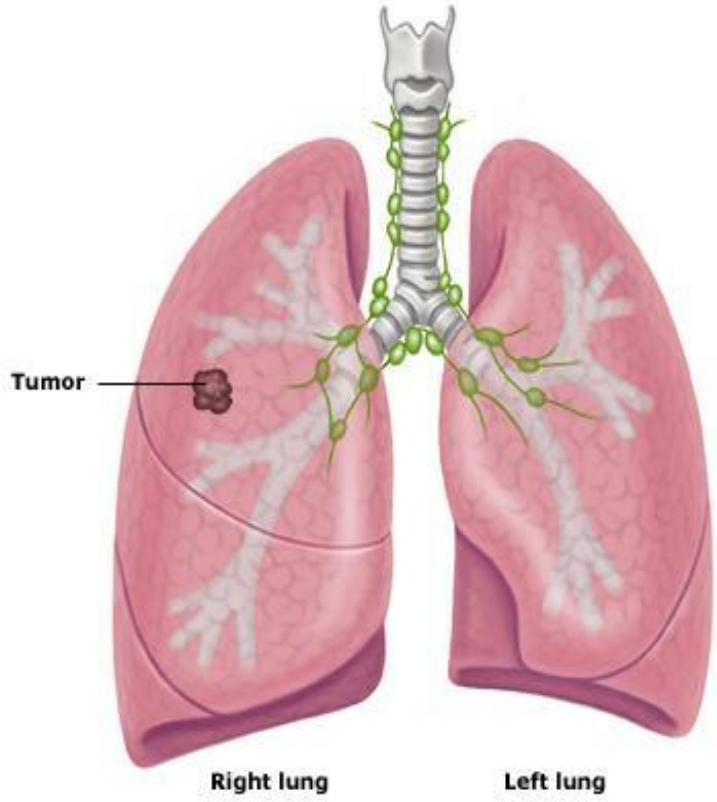
# BRONCHOSCOPY



# Staging



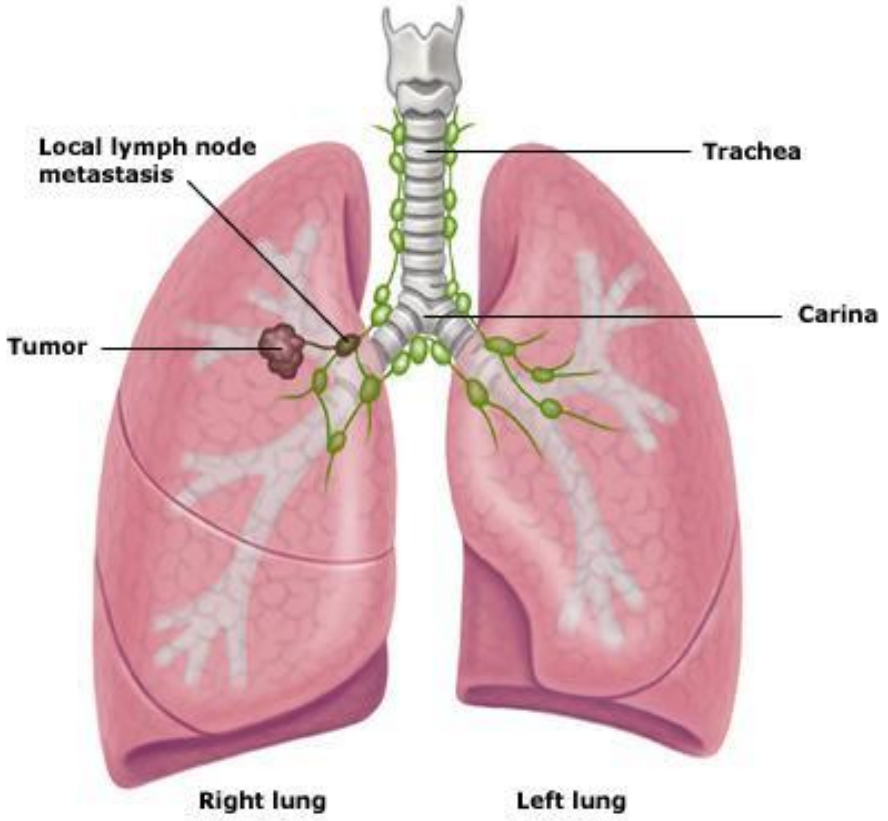
# STAGE I




**Primary tumor in the lung**

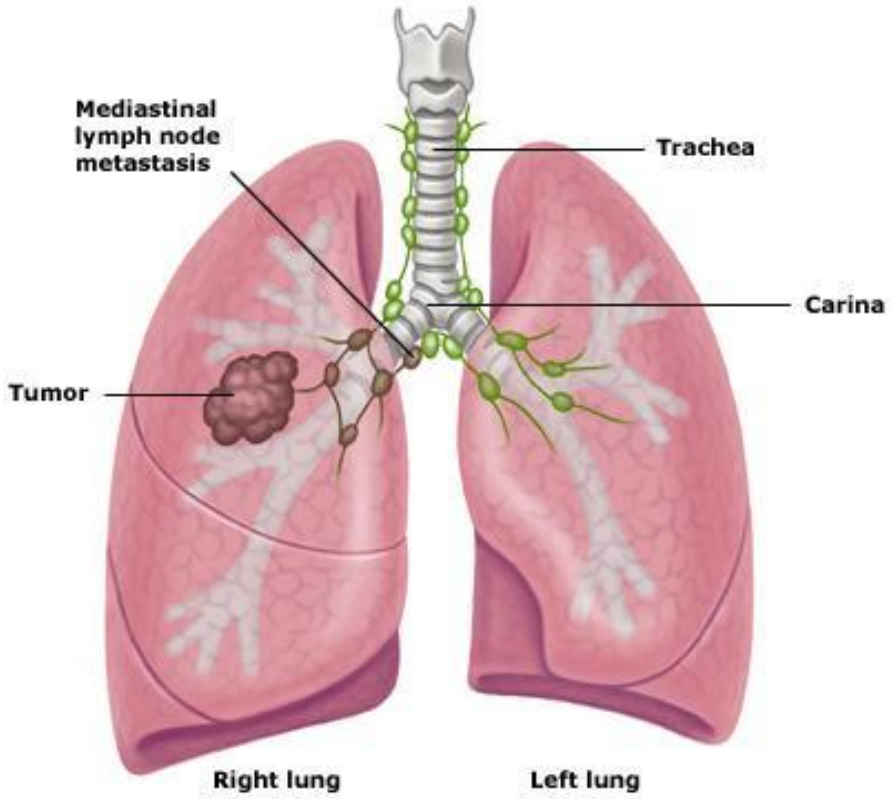
**No lymph nodes involved.**

# STAGE II



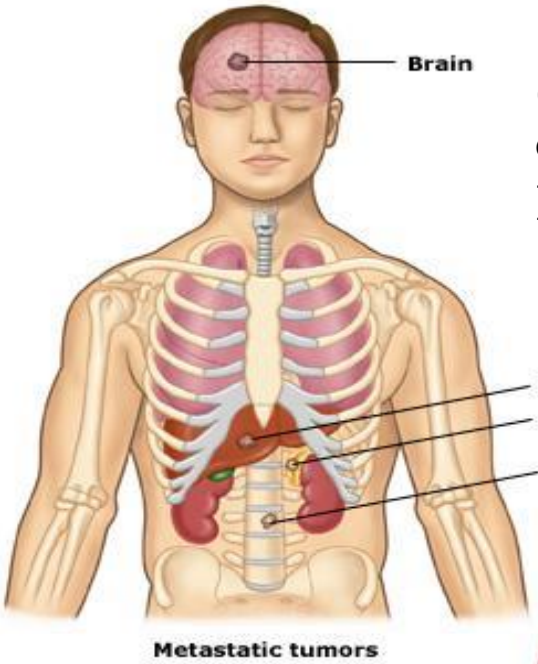

**Primary tumor in the lung and lymph nodes within the lobe or hilum.**

# STAGE III



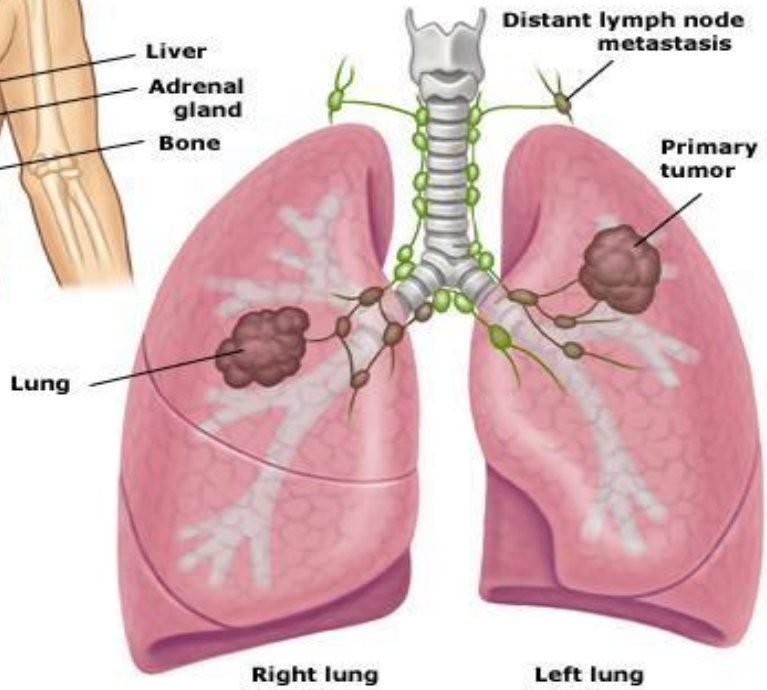

**Locally advanced disease.**
**Mediastinal LN.**
**Primary tumor invades local structures (spine, etc).**

# STAGE IV




**Cancer spread to the other lung or outside the chest.**

**Pleural effusion.**



# TREATMENT

**Operable Early Stage NSCLC** (stage I-IIIA)

Surgical approaches.
Adjuvant chemo.
Adjuvant XRT.

**Advanced NSCLC** (IIIB -IV)

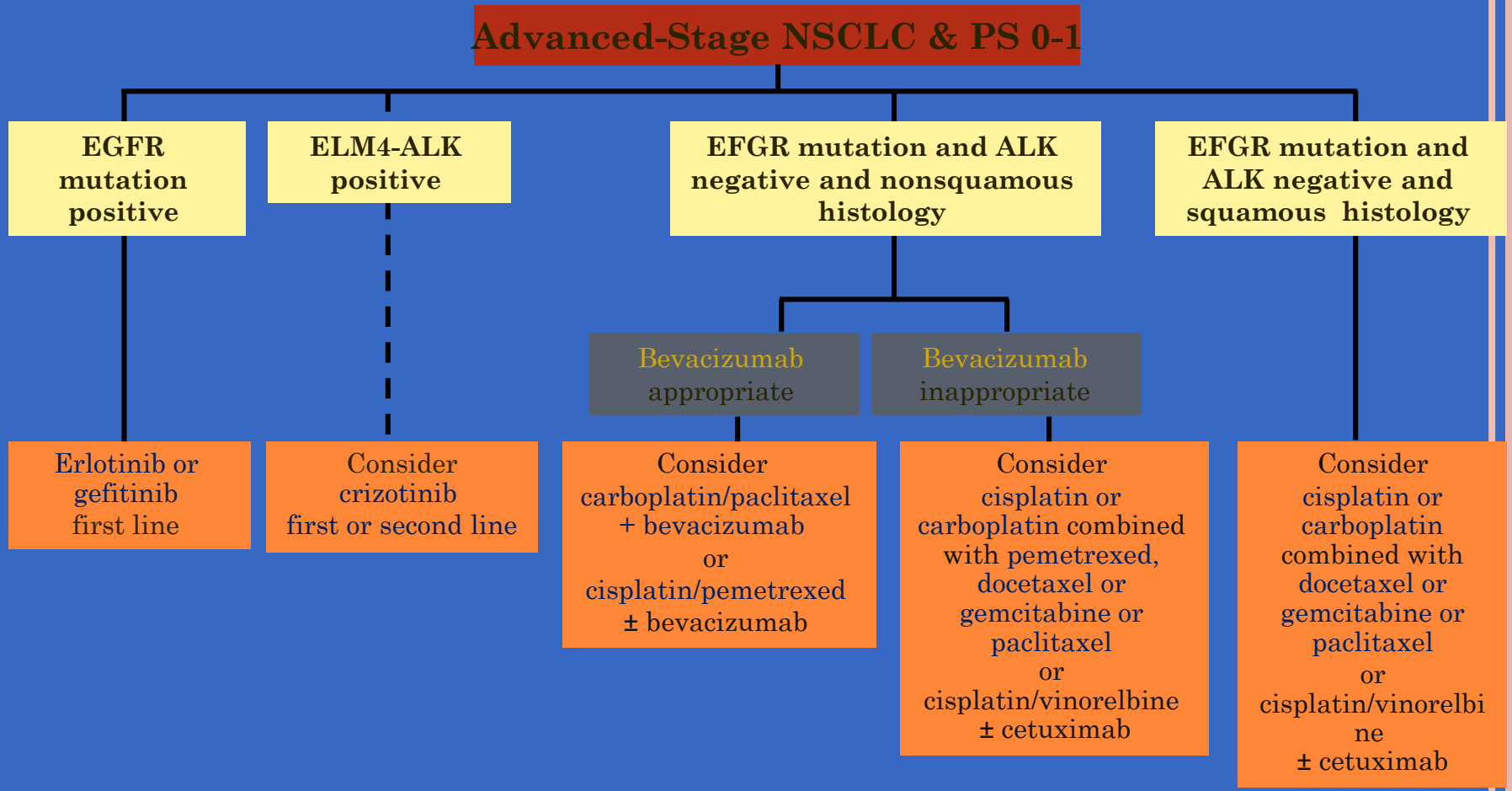
Chemotherapy.

VEGF inhibotors: bevacizumab (Avastin).

EGFR TKI: gefitinib and erlotinib.

ALK: crizotinib.

# Proposed Treatment Algorithm for Advanced NSCLC: First-line Therapy 2012




Updated from Gandara DR, et al. Clin Lung Cancer. 2009;10:392-394.

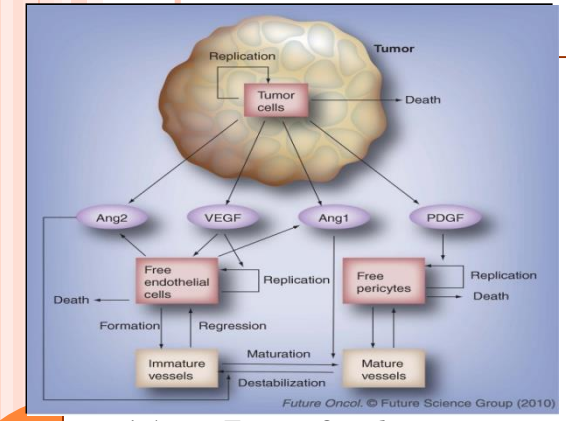
# LEADING QUESTIONS

- How can we assist the oncologist's decisions ?

- Which patient will have better results with a certain treatment ? (main tumor size reduction, less toxicity)

# OPTIMATA

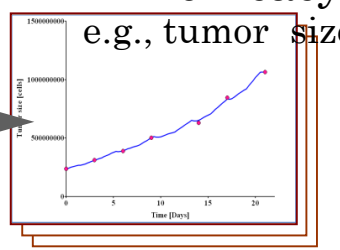
PK/PD mechanistic model for drug



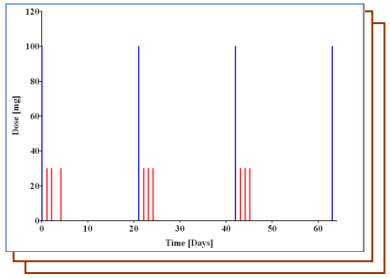

* Agur, Future Oncology 2010

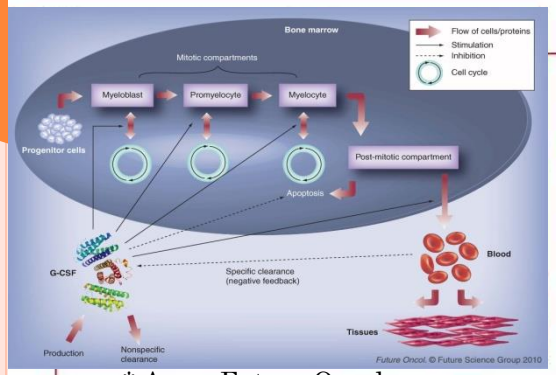
Predict efficacy

e.g., tumor size



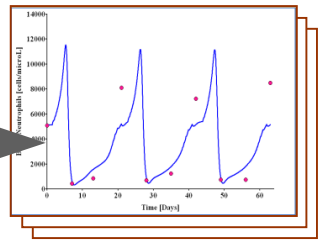
Optimize schedule for mono- or combination therapy






* Agur, Future Oncology 2010

PK/PD mechanistic model for drug toxicity

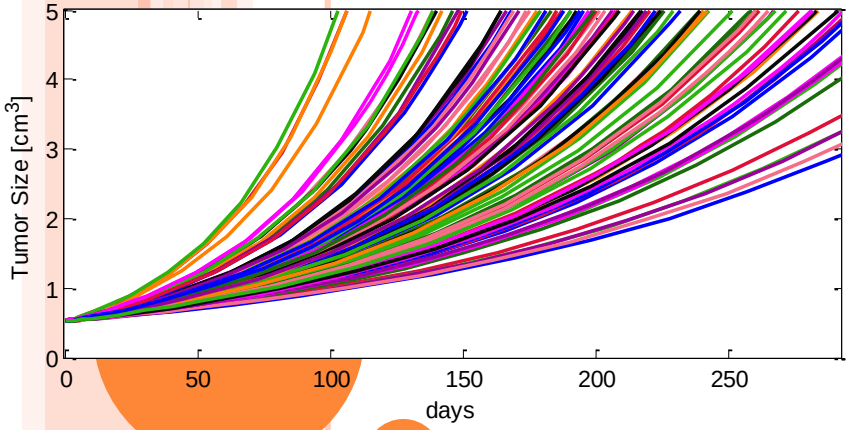


Predict toxicity

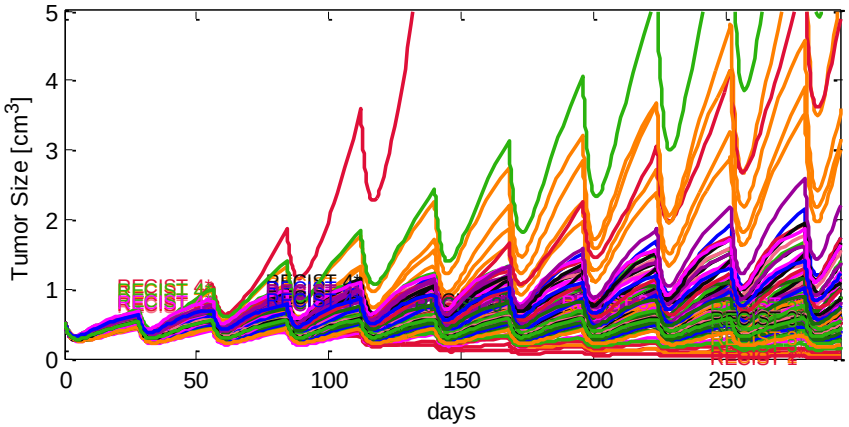
e.g., neutropenia

# OPTIMATA

## *UNTREATED*




## *TREATED*

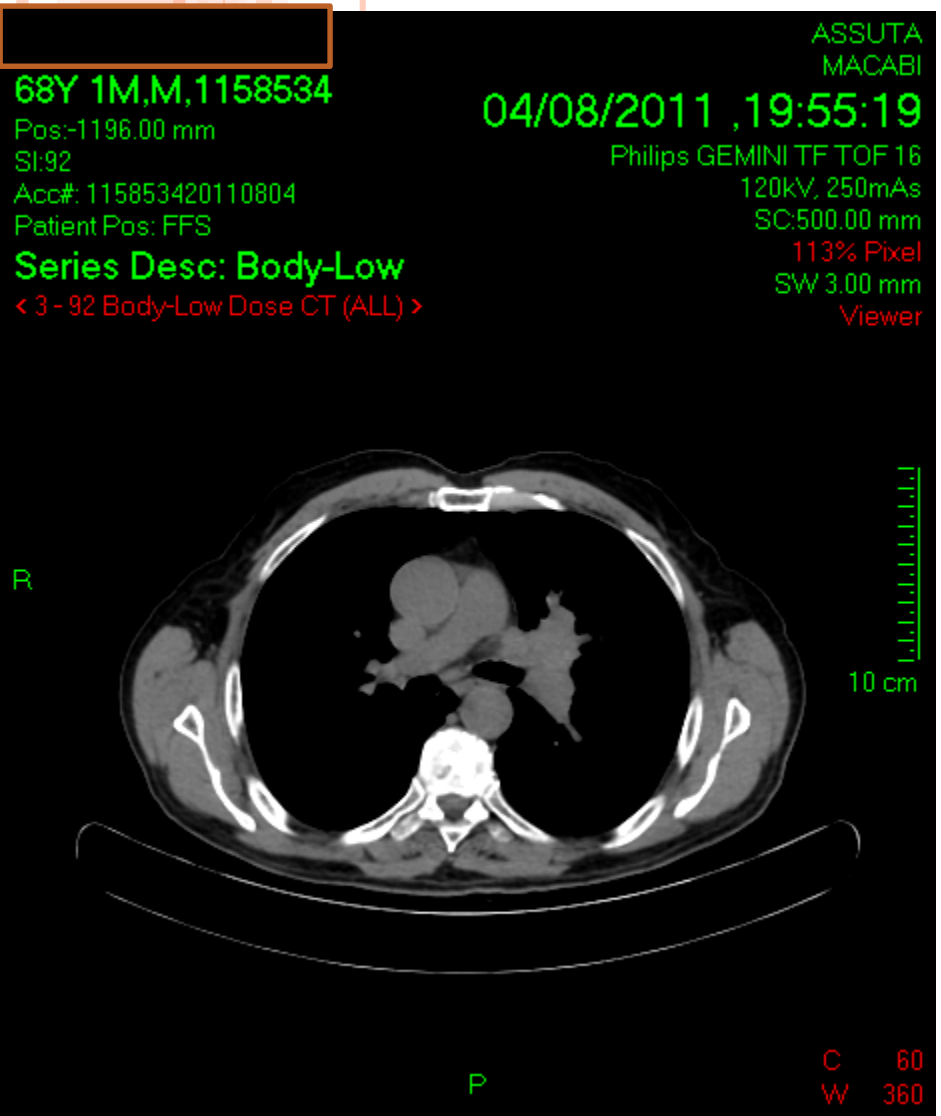


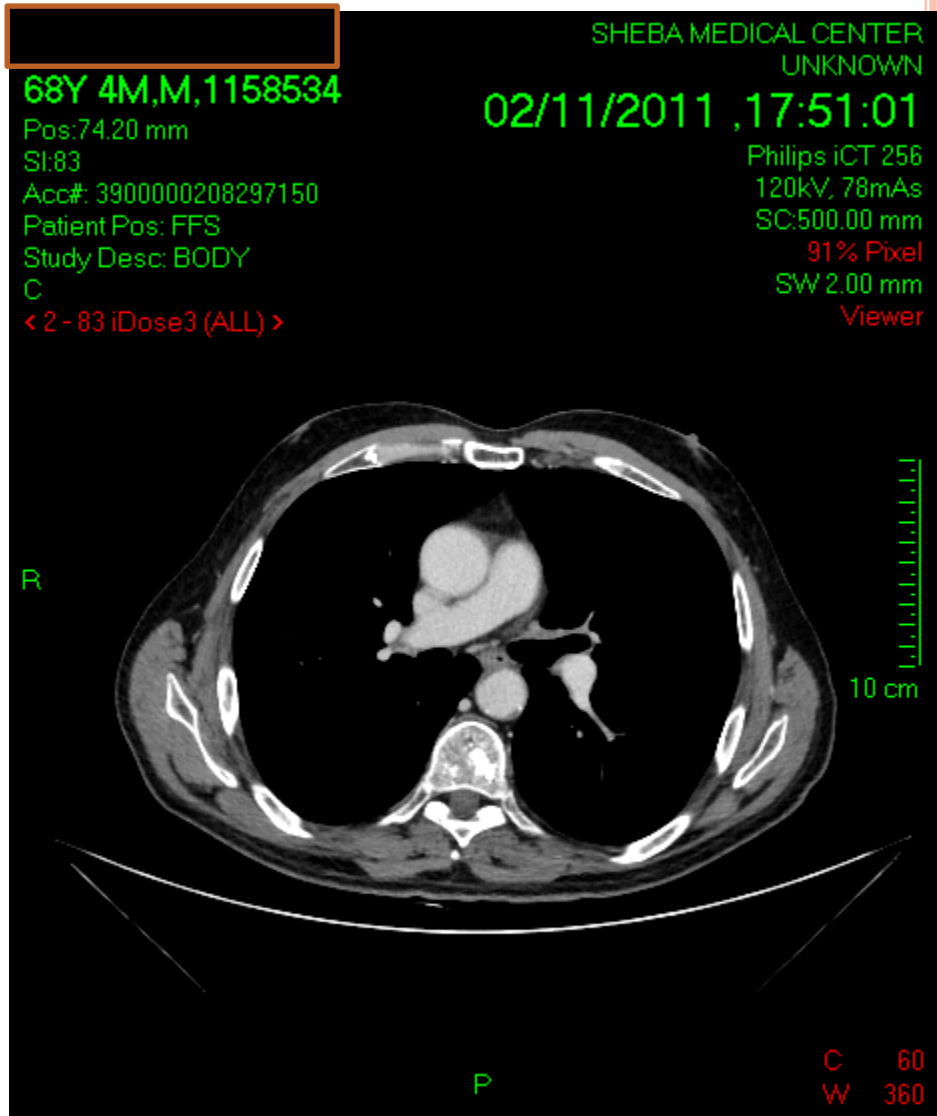
# Research Objective

-Developing this algorithm will address the major need in personalized oncology, particularly in Predicting optimal treatment for individual patients.

We have examined and collected data for 27 patients, that had been treated for NSCLC in the years 2008-2011, in Sheba Medical Center. There are two main protocols we focus on, Cisplatinum+Pemetrexed, (22 patients) and Carboplatin+Paclitaxel (5 patients). Our collected data includes clinical, histological, genetic, and imaging features, as well as blood tests for each patient. Our main objective is an expansion of the database by adding more patients, and by that, validating the algorithm with much greater statistical significance.

# Case study- Partial Response



# Case Study – Stable disease