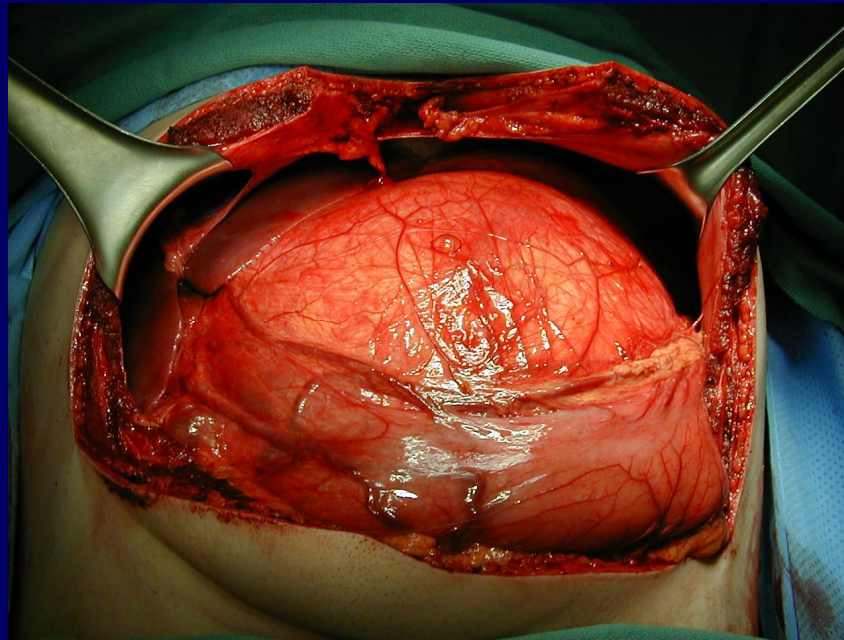


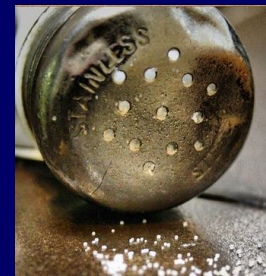
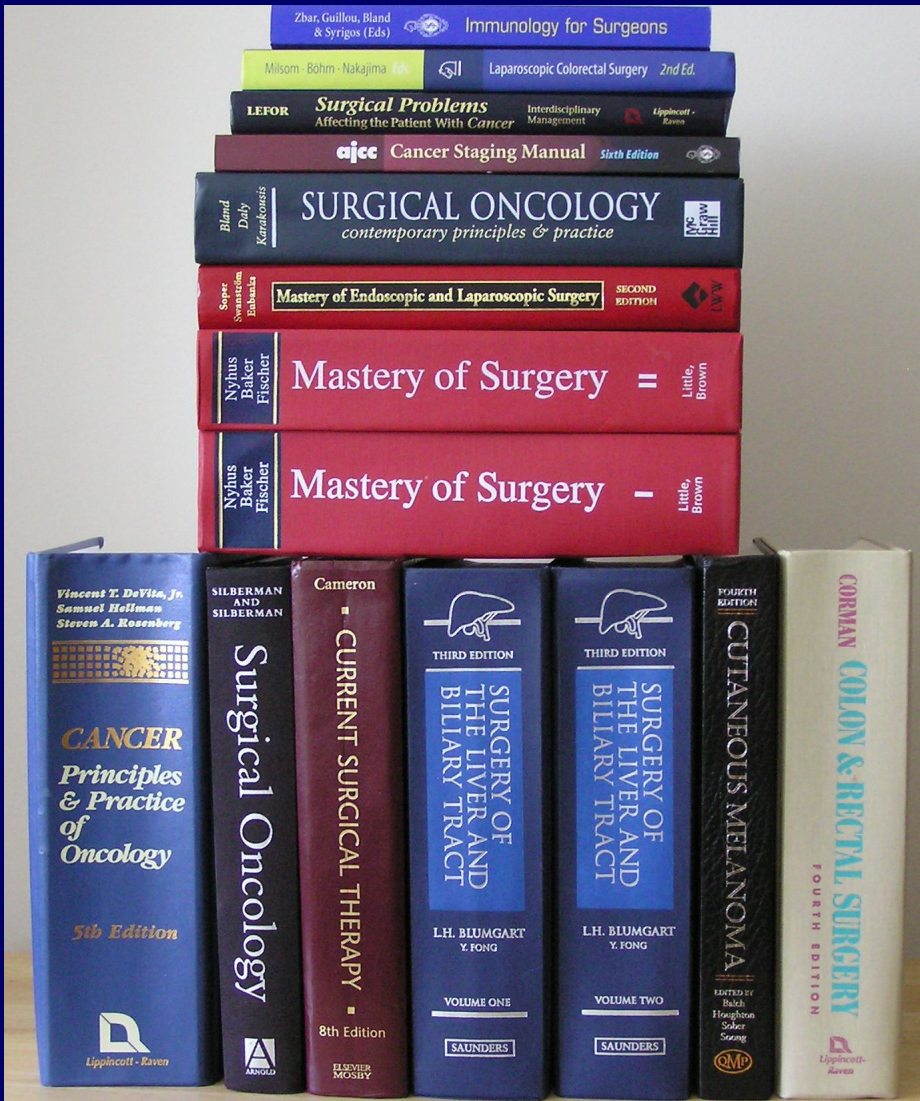
# Principles of Oncologic Surgery



**Surgery Grand Rounds  
August 31, 2009**

**Martin McCarter, M.D.  
Associate Professor of Surgery  
GI Tumor & Endocrine Surgery  
University of Colorado Denver**





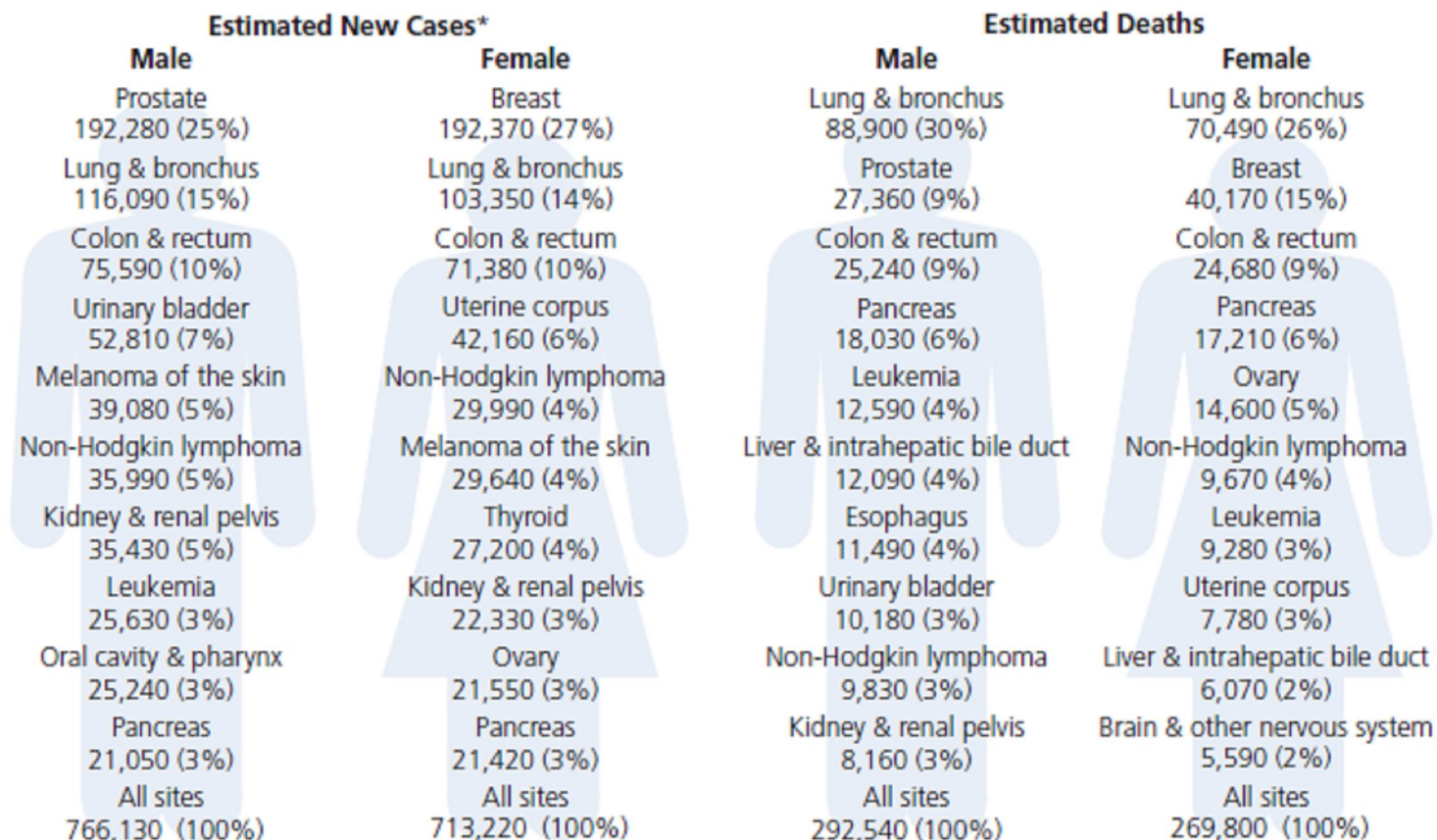
# Principles of Oncologic Surgery

## Outline

- The cancer problem
- Tumor biology
- Tumor staging systems
- General surgical principles
- Integrating multidisciplinary care
- Future of surgical oncology

# Magnitude of the Problem

## Leading Sites of New Cancer Cases and Deaths – 2009 Estimates



\*Excludes basal and squamous cell skin cancers and in situ carcinoma except urinary bladder.

©2009, American Cancer Society, Inc., Surveillance and Health Policy Research

# Scope of the Problem

Probability of Developing Invasive Cancers (%) Over Selected Age Intervals by Sex, US, 2003-2005\*

		Birth to 39	40 to 59	60 to 69	70 and Older	Birth to Death
All sites <sup>†</sup>	Male	1.42 (1 in 70)	8.44 (1 in 12)	15.71 (1 in 6)	37.74 (1 in 3)	43.89 (1 in 2)
	Female	2.07 (1 in 48)	8.97 (1 in 11)	10.23 (1 in 10)	26.17 (1 in 4)	37.35 (1 in 3)
Urinary bladder <sup>‡</sup>	Male	0.02 (1 in 4,448)	0.41 (1 in 246)	0.96 (1 in 104)	3.57 (1 in 28)	3.74 (1 in 27)
	Female	0.01 (1 in 10,185)	0.12 (1 in 810)	0.26 (1 in 378)	1.01 (1 in 99)	1.18 (1 in 84)
Breast	Female	0.48 (1 in 208)	3.79 (1 in 26)	3.41 (1 in 29)	6.44 (1 in 16)	12.03 (1 in 8)
Colon & rectum	Male	0.08 (1 in 1,296)	0.92 (1 in 109)	1.55 (1 in 65)	4.63 (1 in 22)	5.51 (1 in 18)
	Female	0.07 (1 in 1,343)	0.72 (1 in 138)	1.10 (1 in 91)	4.16 (1 in 24)	5.10 (1 in 20)
Leukemia	Male	0.16 (1 in 611)	0.22 (1 in 463)	0.35 (1 in 289)	1.17 (1 in 85)	1.50 (1 in 67)
	Female	0.12 (1 in 835)	0.14 (1 in 693)	0.20 (1 in 496)	0.77 (1 in 130)	1.07 (1 in 94)
Lung & bronchus	Male	0.03 (1 in 3,398)	0.99 (1 in 101)	2.43 (1 in 41)	6.70 (1 in 18)	7.78 (1 in 13)
	Female	0.03 (1 in 2,997)	0.81 (1 in 124)	1.78 (1 in 56)	4.70 (1 in 21)	6.22 (1 in 16)
Melanoma of the skin <sup>§</sup>	Male	0.16 (1 in 645)	0.64 (1 in 157)	0.70 (1 in 143)	1.67 (1 in 60)	2.56 (1 in 39)
	Female	0.27 (1 in 370)	0.53 (1 in 189)	0.35 (1 in 282)	0.76 (1 in 131)	1.73 (1 in 58)
Non-Hodgkin lymphoma	Male	0.13 (1 in 763)	0.45 (1 in 225)	0.58 (1 in 171)	1.66 (1 in 60)	2.23 (1 in 45)
	Female	0.08 (1 in 1,191)	0.32 (1 in 316)	0.45 (1 in 223)	1.36 (1 in 73)	1.90 (1 in 53)
Prostate	Male	0.01 (1 in 10,002)	2.43 (1 in 41)	6.42 (1 in 16)	12.49 (1 in 8)	15.78 (1 in 6)
Uterine cervix	Female	0.15 (1 in 651)	0.27 (1 in 368)	0.13 (1 in 761)	0.19 (1 in 530)	0.69 (1 in 145)
Uterine corpus	Female	0.07 (1 in 1,499)	0.72 (1 in 140)	0.81 (1 in 123)	1.22 (1 in 82)	2.48 (1 in 40)

\*For people free of cancer at beginning of age interval.

†All sites excludes basal and squamous cell skin cancers and in situ cancers except urinary bladder.

‡Includes invasive and in situ cancer cases.

§Statistic is for whites only.

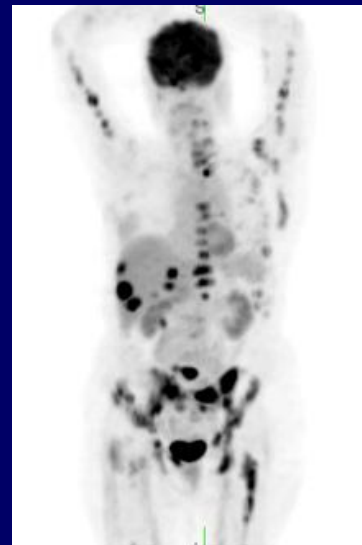
Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.3.0. Statistical Research and Applications Branch, National Cancer Institute, 2008. [srab.cancer.gov/devcan](http://srab.cancer.gov/devcan).

American Cancer Society, Surveillance and Health Policy Research, 2009

# Tumor Biology

Understanding tumor biology is **critical** for:

- deciding when to operate
- deciding what operation to do
- deciding when NOT to operate



# Classes of Tumors

## General Groupings

**Carcinoma = Epithelial tumors**

- breast, melanoma, GI, GU, lung, GYN, H&N
- invade lymphatic and vascular structures

**Sarcoma = Connective tissue tumors**

- displace other structures
- hematogenous spread

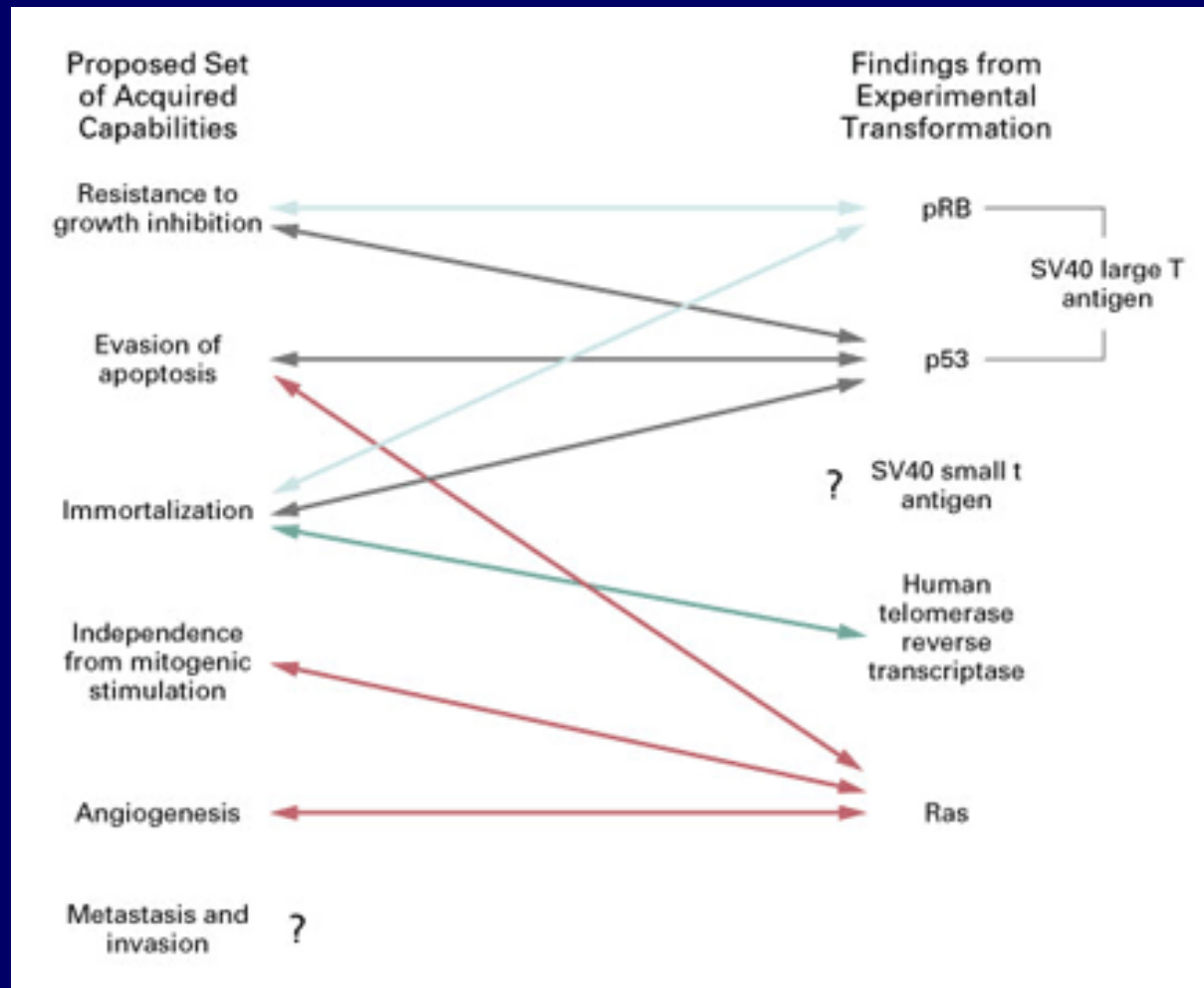
**Ovarian**

**Testicular**

**Carcinoid tumors = “carcinoma like”**

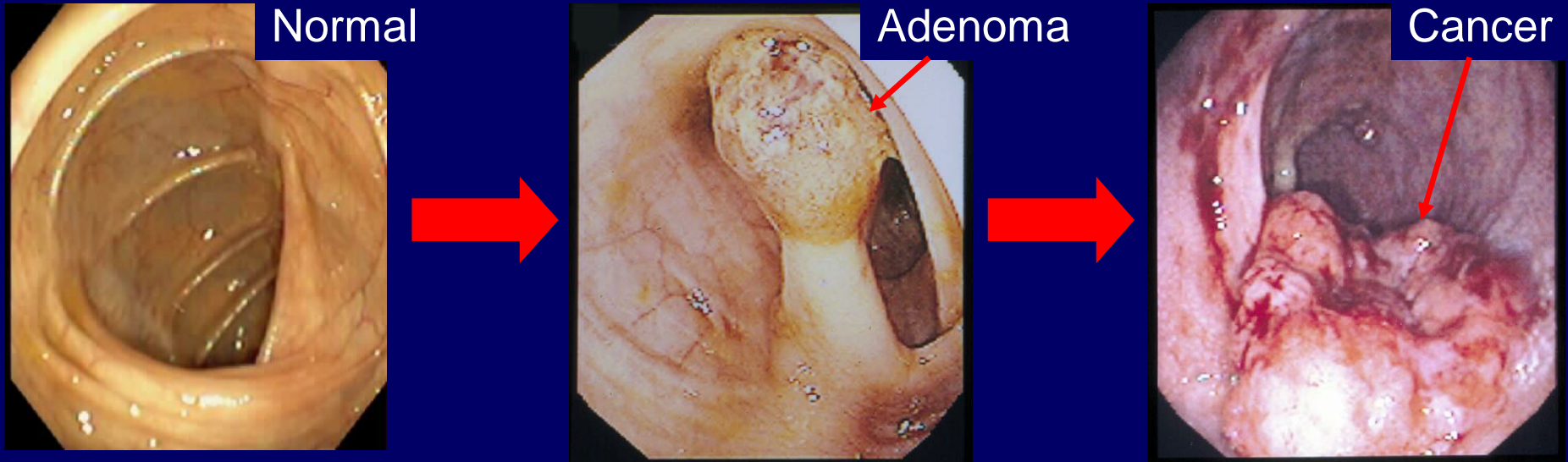
**Liquid tumors – leukemia and lymphoma**

# What Does it Take to Make a Tumor?





# Tumor Biology



APC  
loss

K-ras  
mutation

Chrom 18  
loss

p53  
loss

Normal  
Epithelium

Hyper-  
proliferation

Early  
Adenoma

Intermediate  
Adenoma

Late  
Adenoma

Cancer

# Staging is All About Real Estate

## American Joint Commission on Cancer (AJCC)

T = Tumor (size, grade) N = Nodes (number) M = Metastasis

### Goals

- Estimate prognosis
- Facilitate treatment planning
- Allow comparisons between treatment groups

### General Classification

Stage I -	Superficial early cancer
Stage II -	Locally advanced - nodes
Stage III -	Regionally advanced + nodes
Stage IV -	Metastatic beyond regional nodes

The logo for Coldwell Banker, featuring the words "COLDWELL" and "BANKER" in a bold, sans-serif font, with a small square icon containing a stylized 'C' to the right of "BANKER".

RESIDENTIAL BROKERAGE

# Staging – the TNM System

## Advantages

- Each revision provides more accurate prognosis
- Allows for general estimates of survival

Stage	Est 5 yr Survival
I	95%
II	80%
III	50%
IV	5%

## Disadvantages

- Each revision more complex
- Stage shifting over time
- Still lumping cancers by relatively crude descriptive characteristics

# Cancer Speak

## Terms you may have heard

- **Tumor** = abnormal growth
- **Cancer** = tumor that has the capacity to metastasize
- **Adjuvant therapy** = chemo or radiation therapy added after surgery
- **Neoadjuvant therapy** = chemo or radiation therapy given before planned definitive surgery
- **R0** = complete margin negative resection
- **R1** = complete gross resection, microscopically positive margin
- **R2** = gross disease left behind

# Biology of Cancer Recurrence

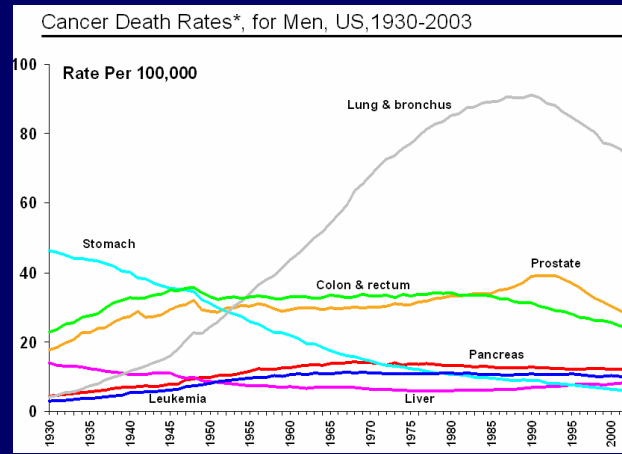
## some general rules of thumb



## Recurrence of tumor

- Tumor environment is a wound that doesn't heal
- ~75% of recurrences occur within the first 2 years of surgery
- 5 year mark for "cure" is arbitrary
  
- One third local recurrence alone
- One third local plus distant simultaneously
- One third distant alone

# Statistics for Cancer Patients



- Median follow-up and survival
- Absolute differences vs. relative differences
- Overall survival
- Disease specific survival
- Disease free survival (recurrence free)

# Surgery as Curative

- To cure a patient with surgery is still relatively rare
- Some percentage (one third?) may be cured
- Earlier detection is best chance for cure
- Clarify the goal of your operation  
(curative, debulking, palliative, preventative)



# Surgery as Preventative

Prophylactic surgery to prevent cancer development

<b>Disease</b>	<b>Marker</b>	<b>Treatment</b>
FAP	APC	Colectomy
MEN 2	RET	Throidectomy
Familial Breast Cancer	BRCA 1,2	Mastectomy
Familial Ovarian Cancer	?	Oophorectomy



# Principles of Surgery for Local Control

- Local control should be a top priority
- First operation is best chance for control
- Apply basic surgical fundamentals to reduce local recurrences
- Salvage surgery to achieve local control problematic



# Principles of Biopsies

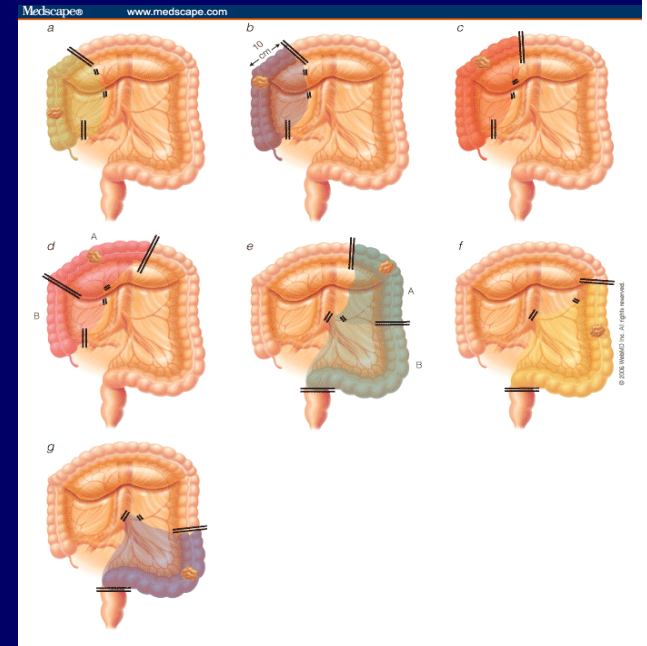
**To biopsy or not to biopsy that is the question?**

**Answer:**

- Know your tumor biology
- Will it change treatment plan?
- Will biopsy cause tumor spread?
- Biopsy options
  - Aspiration, Core, Incisional, Excisional
- Avoid hematoma
- Plan to excise needle or biopsy site

# Principles of Margins

- Factor in tumor biology
- Factor in location
- Factor in other treatments
- In general 1cm gross margin is minimum necessary
- Wider margin preferable if it can be done with minimal additional morbidity
- Goal of margin is reduced local recurrence

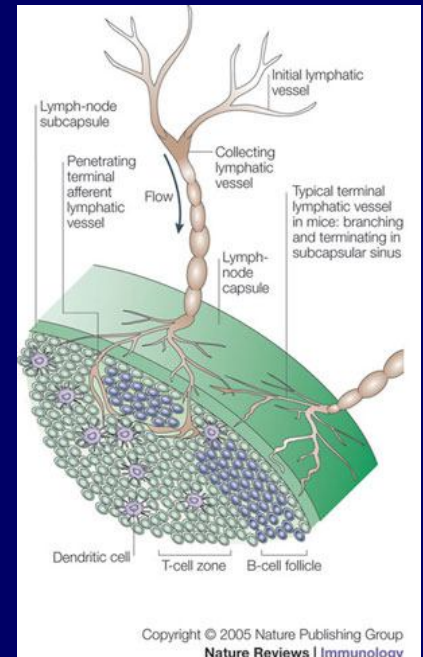


Source: ACS Surgery © 2006 WebMD Inc.

# Principles of Lymph Nodes

## Function of lymph nodes

- Primarily for antigen recognition
- Not a filter
- Majority of tumor cells pass through
- Rare tumor cells can grow in lymph nodes
- Lymph nodes are indicators - not governors - of survival

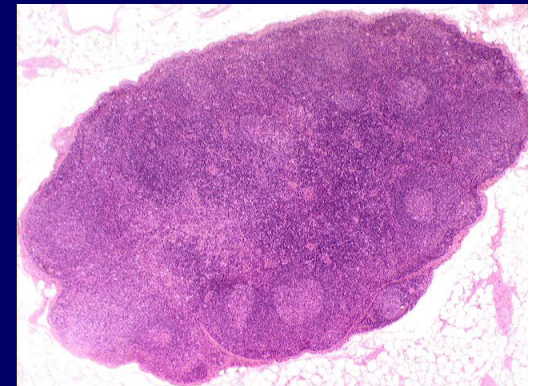
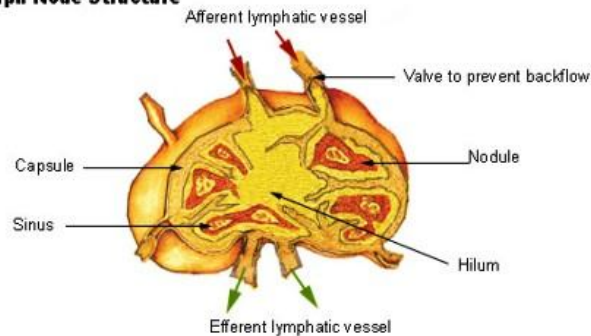


# Principles of Lymph Nodes

## Lymph node dissection

- Harvest lymph nodes for:
  - 1 staging
  - 2 local control
  - 3 interrupt metastatic cascade
- Factor in risk/benefit ratio

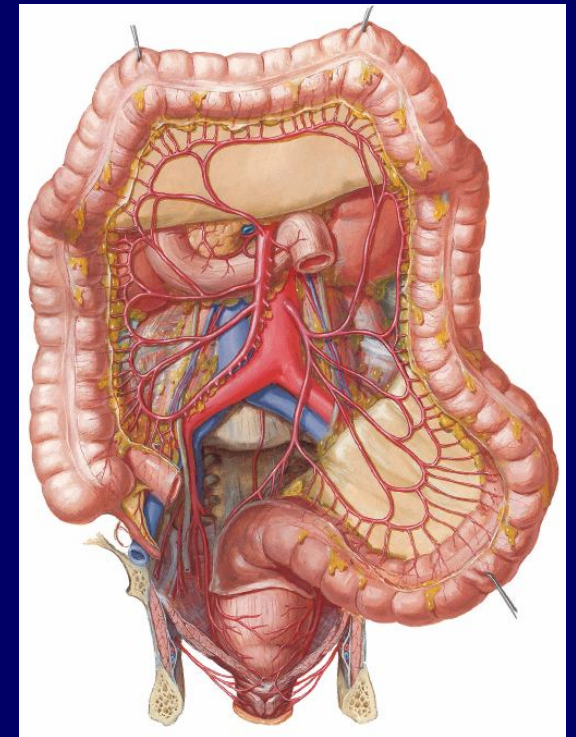
**Lymph Node Structure**



# Principles of Surgical Oncology

## Colorectal cancer

- 5 cm margin when possible
- 1 cm margin for low rectal with XRT
- Take major vascular pedicle at origin along with lymph nodes
- Equivalent cancer outcomes from laparoscopic vs. open



# Principles of Surgical Oncology

## Melanoma

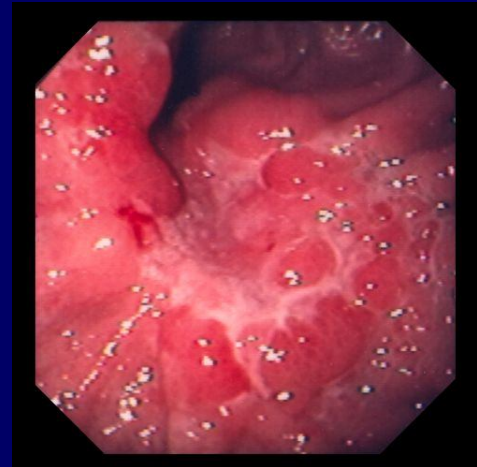
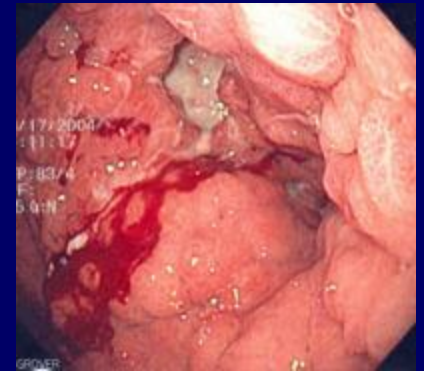
- 1 cm margin for <1mm deep primary
- 2 cm margin for >1mm deep primary
- Exceptions for hands and face
- SLN biopsy for >1mm deep primary
- Sentinel lymph node biopsy for staging
- Lymph node dissection for metastasis



# Principles of Surgical Oncology

## Gastric Cancer

- 5 cm margin when possible
- Take major vascular pedicle with lymph nodes
- Remove lymph node station beyond obviously involved nodes
- Splenectomy generally not indicated
- D2 dissection – no survival benefit

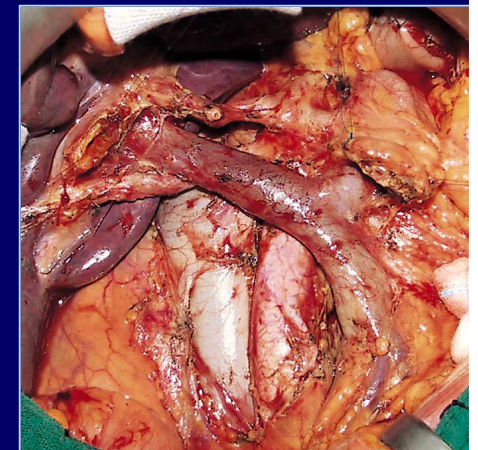
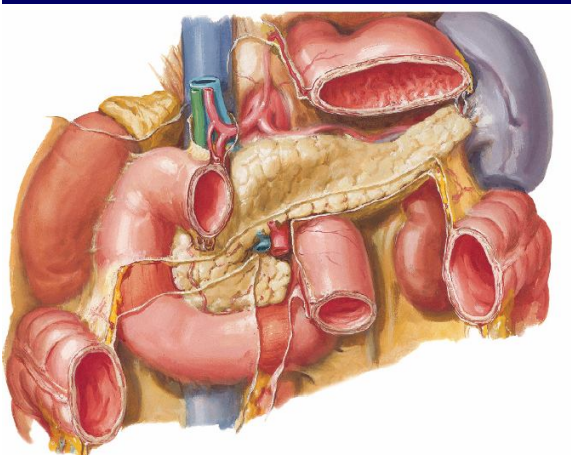
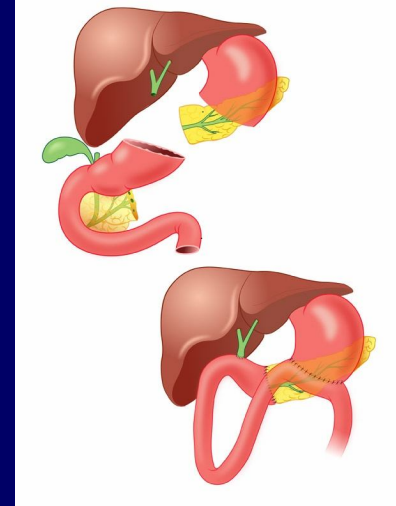




# Principles of Surgical Oncology

## Pancreatic Cancer

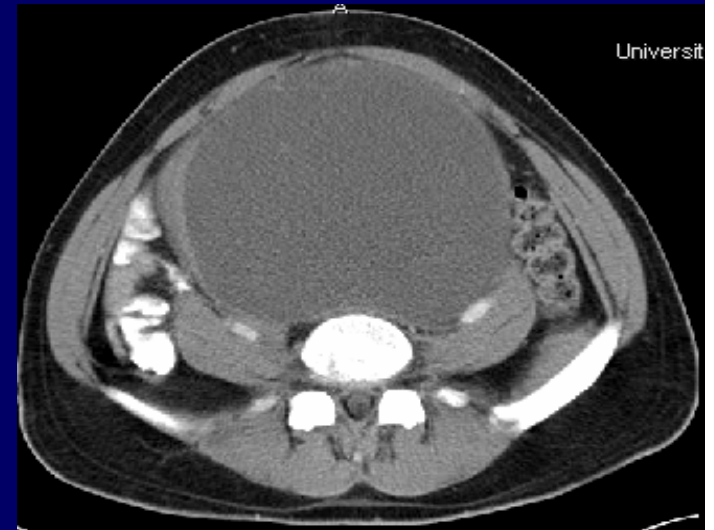
- Resectability is in the eye of the beholder
- Contraindications include Celiac, SMA or Hepatic artery involvement
- Relative contraindications include portal vein or lymph node positive disease



# Principles of Surgical Oncology

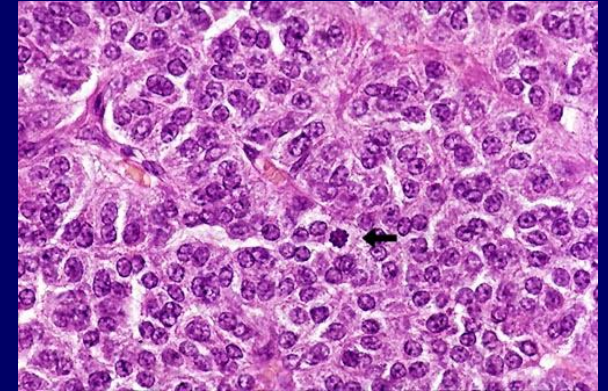
## Sarcomas

- 1-2 cm gross margin
- Preserve neurovascular structures
- No need for lymph nodes\*
- Radiation reduces local recurrence
- Chemotherapy of limited value



# Principles of Surgical Oncology

## Carcinoids

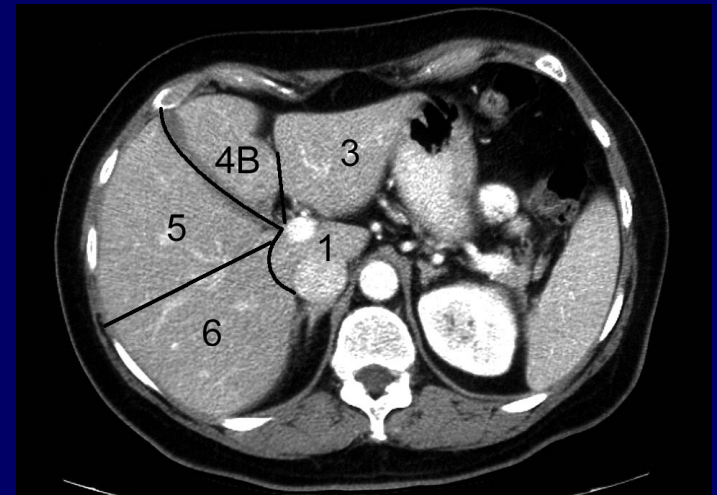


- Slow growing
- Surgery for symptoms – obstruction, hormonal
- Debulking as a goal
- <1 cm – remove tumor only
- >2 cm – remove tumor and lymph nodes
- 1-2 cm – consider removing lymph nodes

# Principles of Surgical Oncology

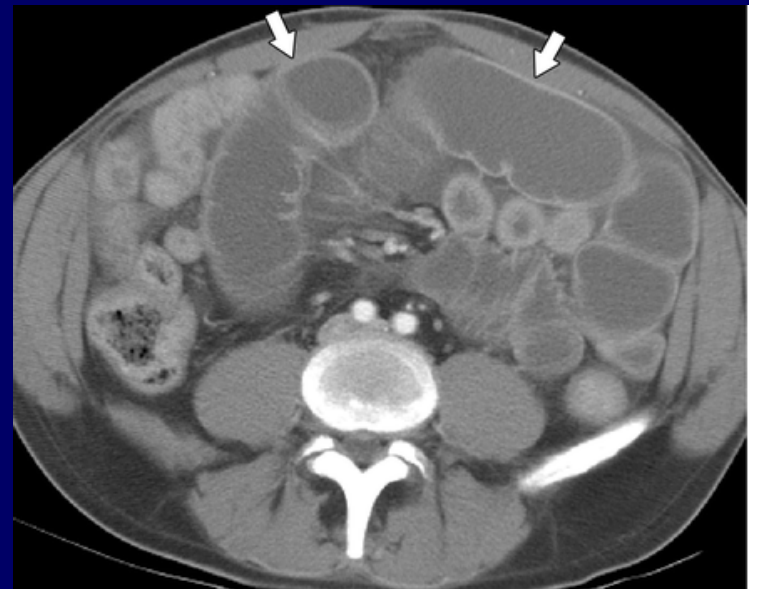
## Liver Tumors

- Primary vs. metastatic
- Resectability
  - Eye of the beholder
  - Real estate
  - Defined by what will be left behind  
(not by what can be removed)



# Principles of Palliative Surgery

- One cannot palliate asymptomatic cancer patients
- Address the highest priority symptom
- Manage expectations
- 25% will fail immediately
- 25% will recur with same symptom



# Principles of Radiation Oncology

## Radiation Therapy

- Rapidly dividing cells
- Can help reduce local recurrence rate
- Organ preservation (breast, larynx, anal sphincter, extremity)
- Technology and targeting improving

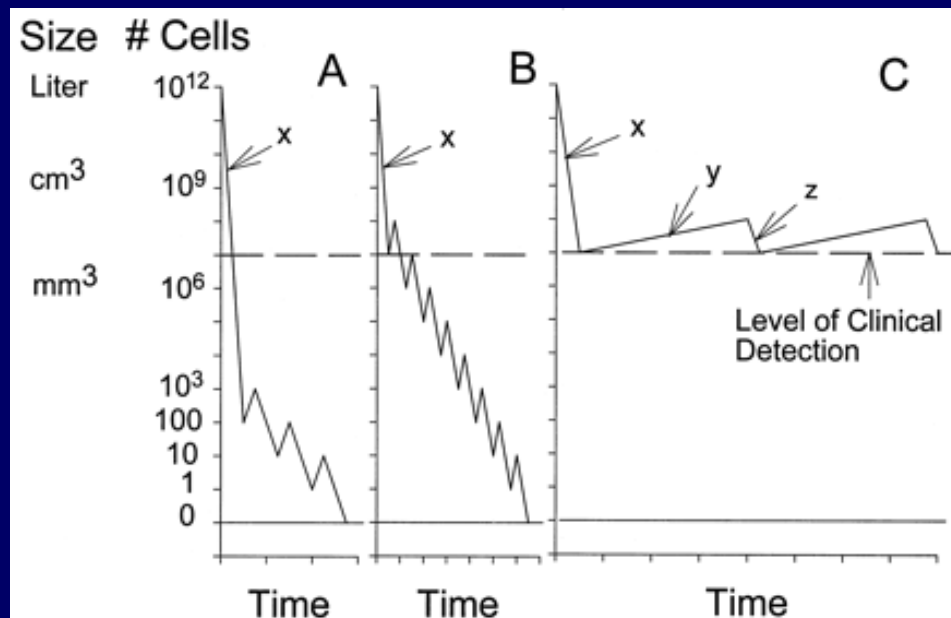
Breast cancer  
Prostate cancer  
Rectal cancer  
Head & Neck  
Sarcomas



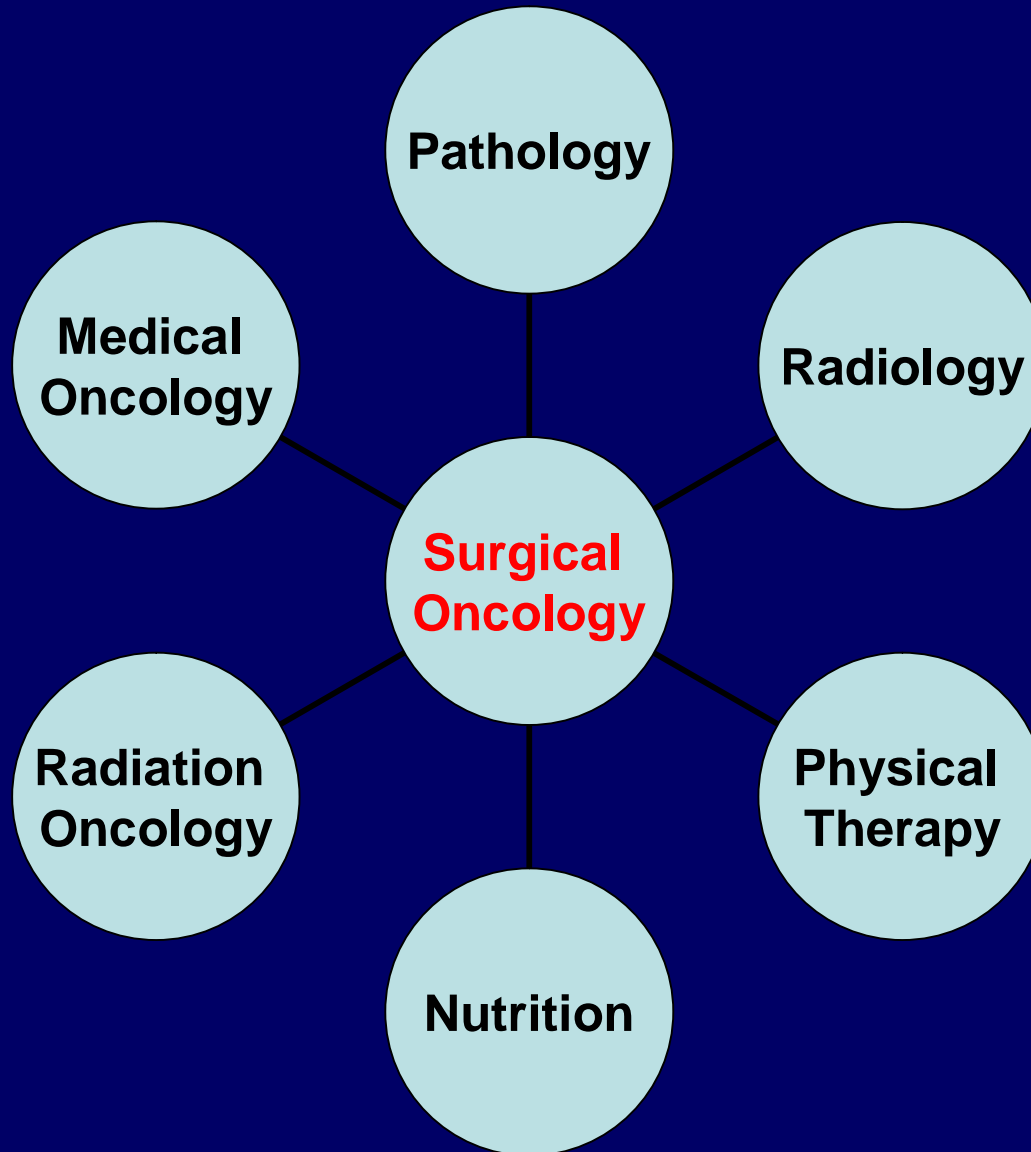
# Principles of Medical Oncology

## Concepts of Chemotherapy

- Tumor doubling time
- Adjuvant vs. Neoadjuvant
- Targeting molecular pathways
- Biologic response indicators
- Drug development – phase I, II, III



# Integrating a Multidisciplinary Approach

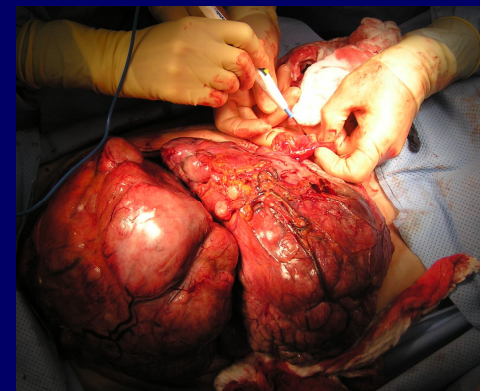




# Future of Surgical Oncology “Targeted Therapy”

## The paradigm of Gastrointestinal Stromal Tumors (GIST)

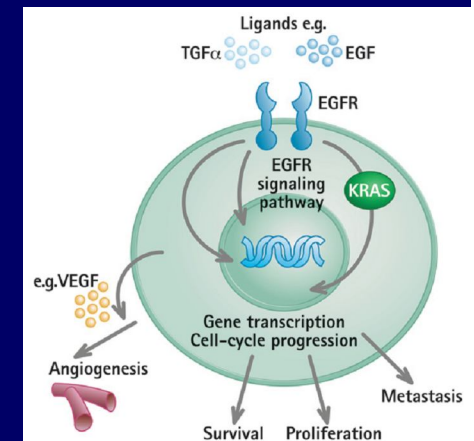
- cKIT mutation (tyrosine kinase) identified as the activating growth signal
- Imatinib (Gleevec) developed as an oral agent to block the activating mutation (ATP binding site)
- Indicated in metastatic and high risk resected GIST
- Changed the natural history of this disease



# Future of Surgical Oncology “Personalized Therapy”

## Example of Tumor KRAS Status in Colorectal Cancer

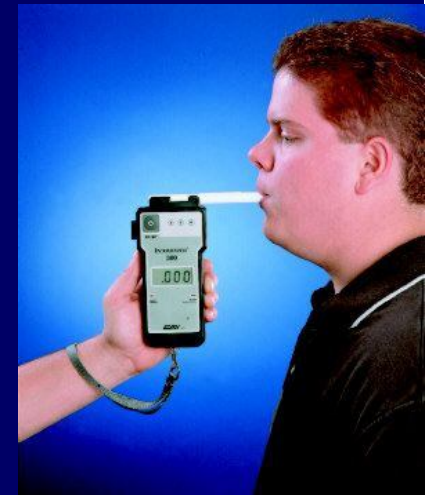
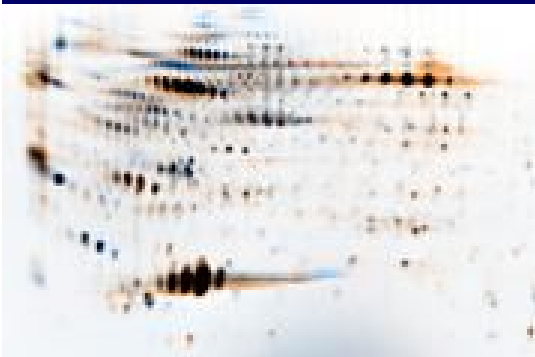
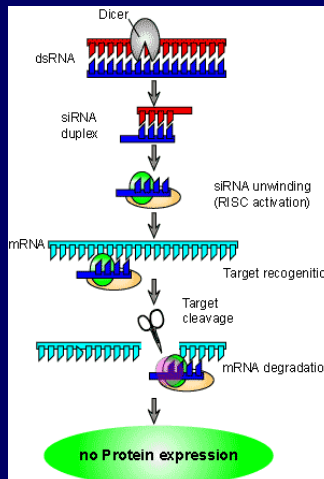
- Cetuximab (Erbitux) and panitumumab (Vectibix) are monoclonal antibodies directed at the epidermal growth-factor receptor
- Approved for treating metastatic colorectal cancer
- Recent trials demonstrated that tumors with a mutation in KRAS do not respond to EGFR receptor blockade
- Tumor analysis now required to treat with these agents



# Future of Surgical Oncology Biomarkers

**Biomarkers are tumor or circulating molecules that help detect and monitor certain cancers**

- CEA, CA19-9, PSA, CA27-29
- Proteomic analysis
- microRNA or small interfering RNA (siRNA) analysis
- Breath analysis



# Fundamentals of Surgical Oncology

**Biology is King**

**Selection is Queen**

**Technical maneuvers are the  
Prince and Princess**

Occasionally the prince and princess try to overthrow the powerful forces of the King and Queen, sometimes with temporary apparent victories, usually to no long term avail.

Blake Cady, MD

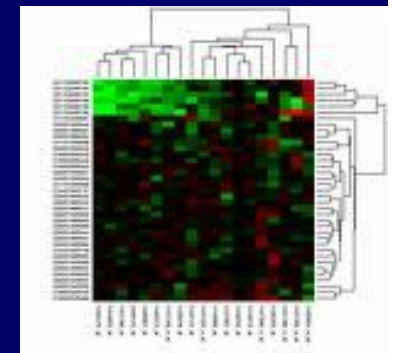






# Future of Surgical Oncology

- Growing opportunity
- 1 in 3 diagnosed with some form of cancer
- Aging population
- Increased need for surgical specialists with broad knowledge of cancer treatments
- Integration of multiple therapies
- Field wide open for basic and clinical research
- Intellectually stimulating – rapid progress
- Molecular evaluation of tumor





# Rules of Surgical Oncology

**Biology is King**

**Selection is Queen**

**Technical maneuvers are the  
Prince and Princess**

Occasionally the prince and princess try to overthrow the powerful forces of the King and Queen, sometimes with temporary apparent victories, usually to no long term avail.

Blake Cady, MD

# #1 Rule of Surgical Oncology

When in doubt – consult this man



# Future of Surgical Oncology

**Past**

**Radical resection**

**Present**

**Conservative resection  
(laparoscopic approaches)**

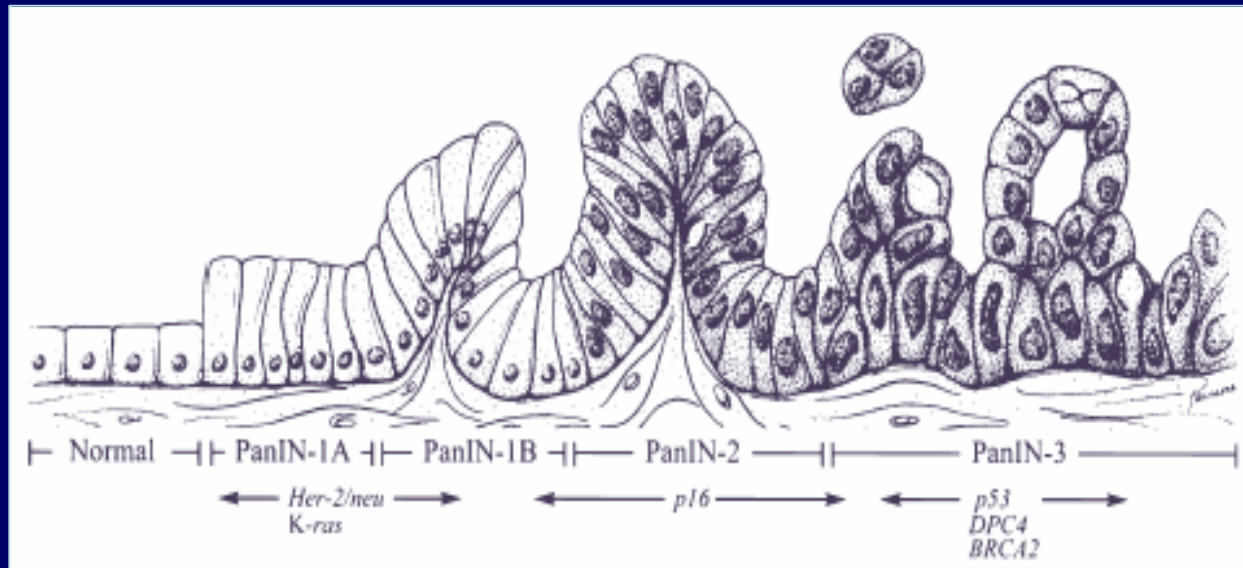
**Future**

**?**

# Tumor Biology

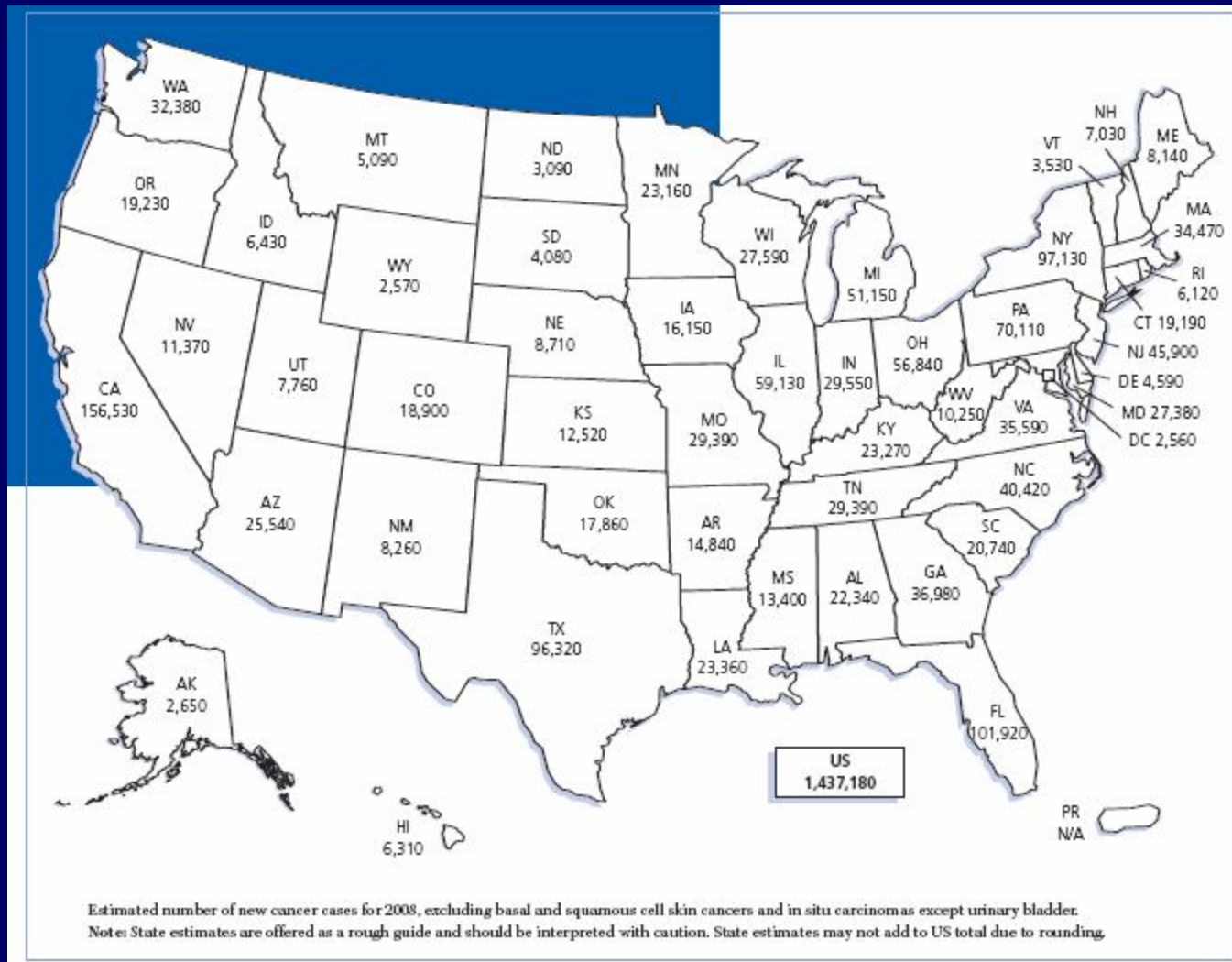
<b>Tumor Type</b>	<b>Estimated Tumor Doubling Time (days)</b>
<b>Choriocarcinoma</b>	<b>1.5</b>
<b>ALL</b>	<b>4-6</b>
<b>Hodgkin's</b>	<b>38</b>
<b>GI adenocarcinoma</b>	<b>80-130</b>

# Molecular Events in Pancreatic Cancer



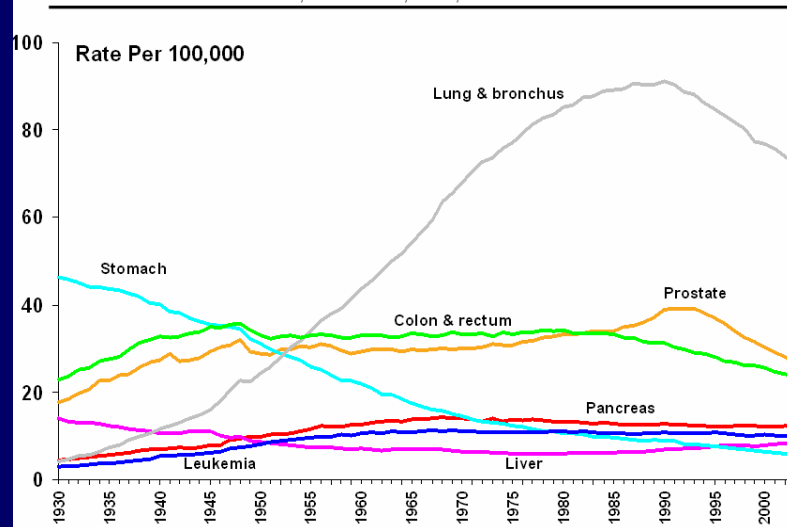
- **Oncogene activation/overexpression**
  - **K-ras (85%)**
- **Receptor tyrosine kinase overexpression**
  - HER2/neu
  - EGFR
- **Tumor suppressor mutation**
  - p53 (50%)
  - SMAD4 (DPC4) (50%)
- **Cell cycle regulatory protein silencing/loss**
  - p16 (8%)
- **Nuclear Transcription Factor Activation**

# Scope of the Problem

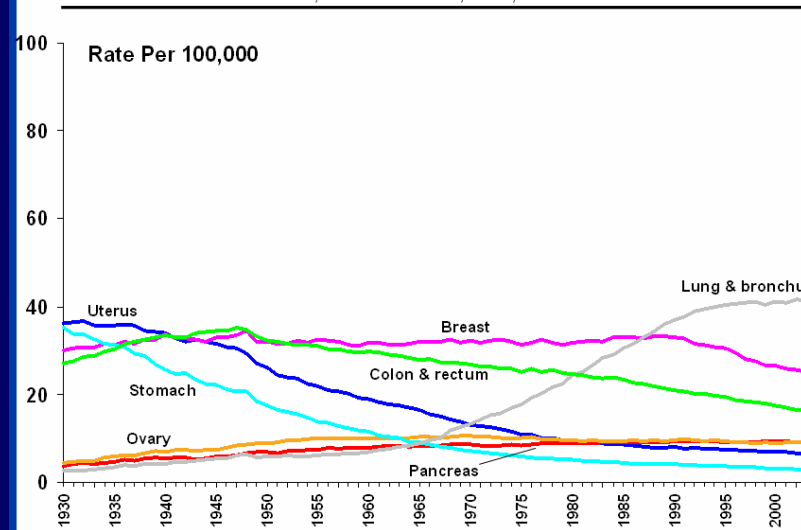


# Scope of the Problem

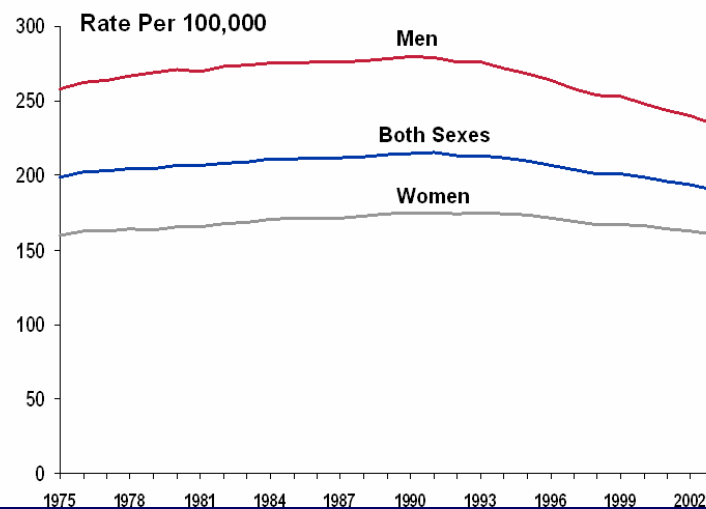
Cancer Death Rates\*, for Men, US, 1930-2003



Cancer Death Rates\*, for Women, US, 1930-2003

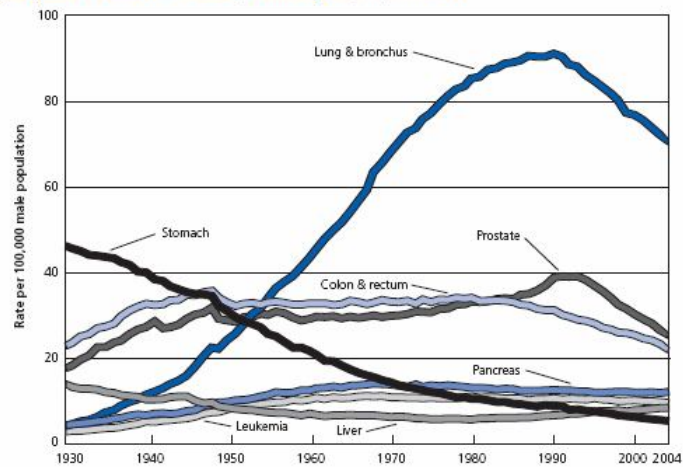


Cancer Death Rates\*, All Sites Combined, All Races, US, 1975-2003



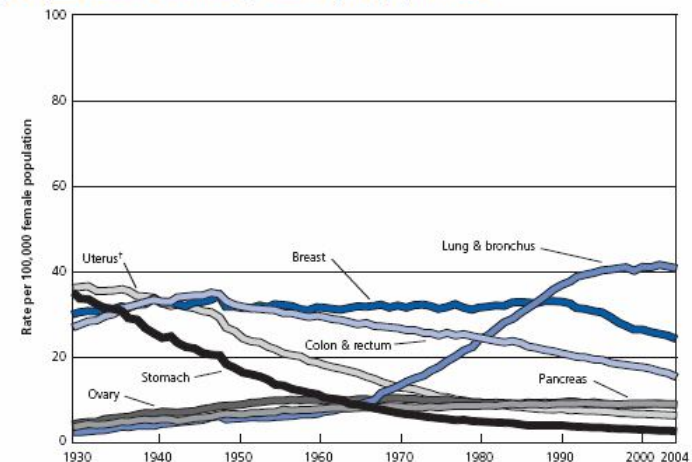
# Scope of the Problem

Age-Adjusted Cancer Death Rates,\* Males by Site, US, 1930-2004



\*Per 100,000, age-adjusted to the 2000 US standard population.  
 Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, and colon and rectum are affected by these coding changes.  
 Source: US Mortality Data 1960 to 2004, US Mortality Volumes 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006.  
 American Cancer Society, Surveillance Research, 2008

Age-Adjusted Cancer Death Rates,\* Females by Site, US, 1930-2004

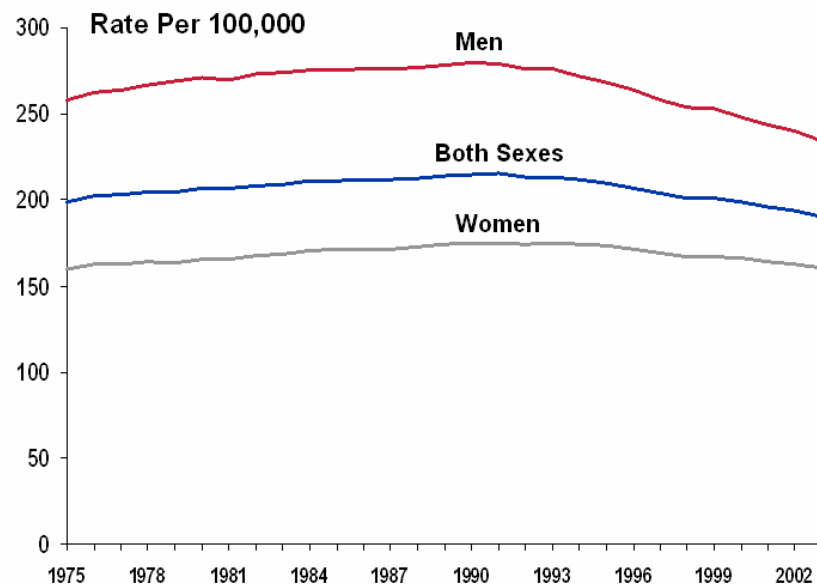


\*Per 100,000, age-adjusted to the 2000 US standard population. †Uterus cancer death rates are for uterine cervix and uterine corpus combined.  
 Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the lung and bronchus, colon and rectum, and ovary are affected by these coding changes.  
 Source: US Mortality Data 1960 to 2004, US Mortality Volumes 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006.  
 American Cancer Society, Surveillance Research, 2008



# Scope of the Problem

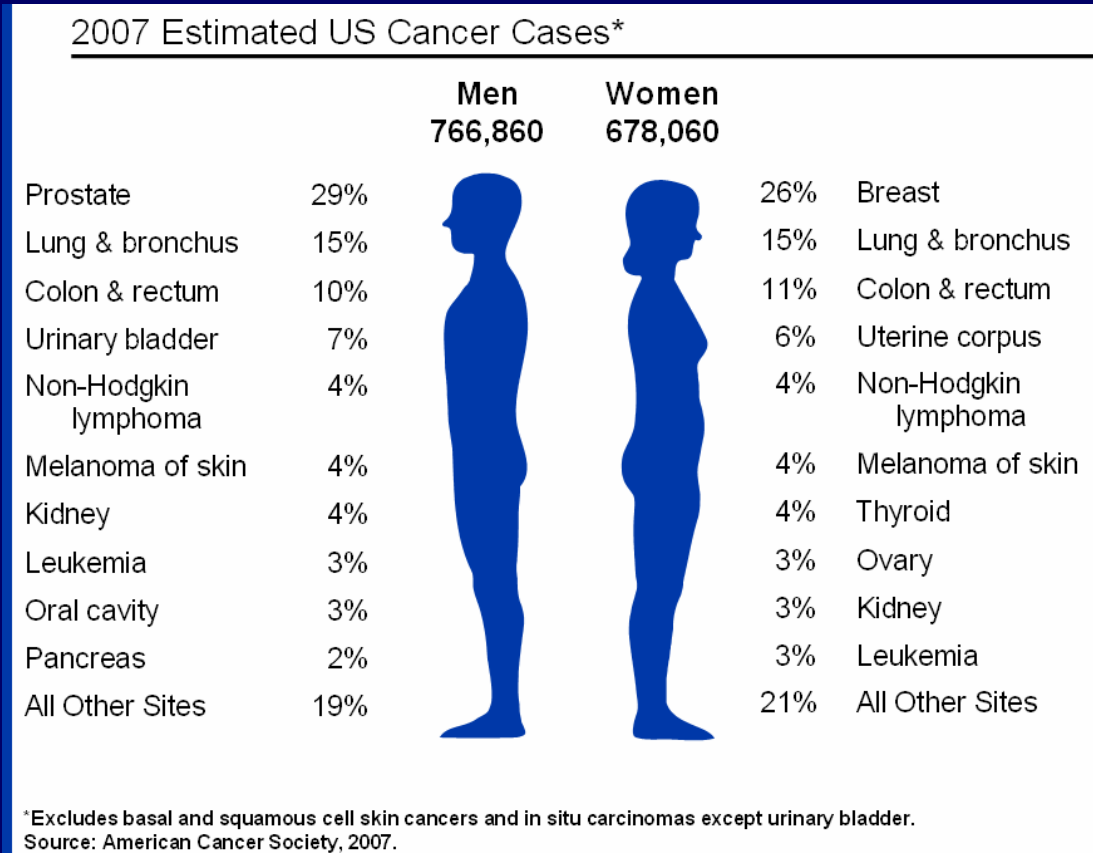
Cancer Death Rates\*, All Sites Combined, All Races, US, 1975-2003



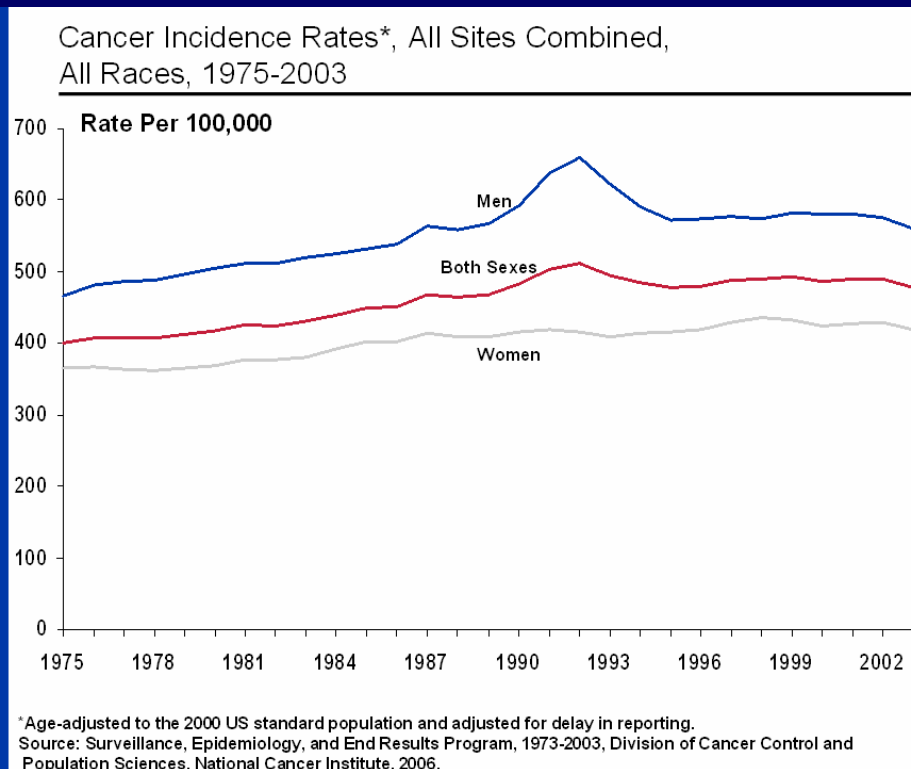
\*Age-adjusted to the 2000 US standard population.

Source: Surveillance, Epidemiology, and End Results (SEER) Program ([www.seer.cancer.gov](http://www.seer.cancer.gov)) SEER\* Stat Database: Mortality - All COD, Public-Use With State, Total U.S. (1969-2003), National Cancer Institute, DCCP Surveillance Research Program, Cancer Statistics Branch, released April 2006. Underlying mortality data provided by NCHS ([www.cdc.gov/nchs](http://www.cdc.gov/nchs)).

# Scope of the Problem



# Scope of the Problem



# Scope of the Problem

Five-year Relative Survival (%)\* during Three Time Periods  
By Cancer Site

Site	1975-1977	1984-1986	1996-2002
All sites	50	53	66
Breast (female)	75	79	89
Colon	51	59	65
Leukemia	35	42	49
Lung and bronchus	13	13	16
Melanoma	82	86	92
Non-Hodgkin lymphoma	48	53	63
Ovary	37	40	45 <sup>†</sup>
Pancreas	2	3	5
Prostate	69	76	100
Rectum	49	57	66
Urinary bladder	73	78	82

\*5-year relative survival rates based on follow up of patients through 2003.

<sup>†</sup>Recent changes in classification of ovarian cancer have affected 1996-2002 survival rates.

Source: Surveillance, Epidemiology, and End Results Program, 1975-2003, Division of Cancer Control and Population Sciences, National Cancer Institute, 2006.

# Principles of Patient Selection

- Know tumor biology
- Know extent of disease
- Disease free interval
- Clarify goal of operation  
(cure, debulk, palliate)

# Patient Selection - Liver Metastasis

## Risk Factors

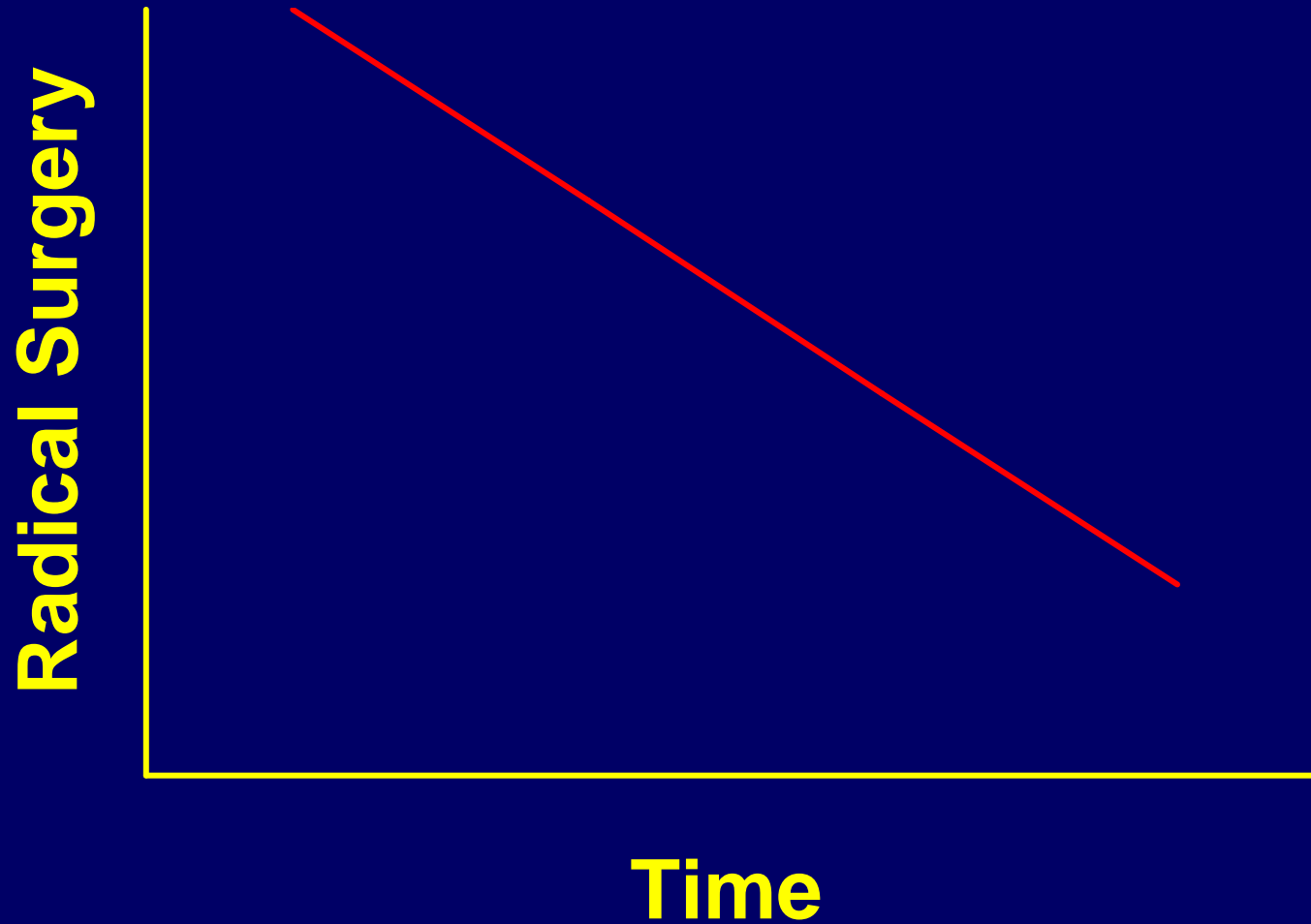
- Node positive primary
- Disease free interval <12 mo
- >1 tumor
- Size >5cm
- CEA > 200ng/ml

**Table 5. CLINICAL RISK SCORE FOR TUMOR RECURRENCE**

Score	Survival (%)					Median (mo)
	1-yr	2-yr	3-yr	4-yr	5-yr	
0	93	79	72	60	60	74
1	91	76	66	54	44	51
2	89	73	60	51	40	47
3	86	67	42	25	20	33
4	70	45	38	29	25	20
5	71	45	27	14	14	22

Each risk factor is one point: node-positive primary, disease-free interval <12 months, >1 tumor, Size >5 cm, CEA >200 ng/ml.

# History of Surgical Oncology



# Scope of the Problem

Lifetime Probability of Developing Cancer, by Site, Women, US, 2001-2003\*

Site	Risk
All sites†	1 in 3
Breast	1 in 8
Lung & bronchus	1 in 16
Colon & rectum	1 in 19
Uterine corpus	1 in 40
Non-Hodgkin lymphoma	1 in 55
Ovary	1 in 69
Melanoma	1 in 73
Pancreas	1 in 79
Urinary bladder‡	1 in 87
Uterine cervix	1 in 138

\* For those free of cancer at beginning of age interval. Based on cancer cases diagnosed during 2001 to 2003.  
 † All Sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.  
 ‡ Includes invasive and in situ cancer cases  
 Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.1.1 Statistical Research and Applications Branch, NCI, 2006. <http://srab.cancer.gov/devcan>

Lifetime Probability of Developing Cancer, by Site, Men, 2001-2003\*

Site	Risk
All sites†	1 in 2
Prostate	1 in 6
Lung and bronchus	1 in 12
Colon and rectum	1 in 17
Urinary bladder‡	1 in 28
Non-Hodgkin lymphoma	1 in 47
Melanoma	1 in 49
Kidney	1 in 61
Leukemia	1 in 67
Oral Cavity	1 in 72
Stomach	1 in 89

\* For those free of cancer at beginning of age interval. Based on cancer cases diagnosed during 2001 to 2003.  
 † All Sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.  
 ‡ Includes invasive and in situ cancer cases  
 Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.1.1 Statistical Research and Applications Branch, NCI, 2006. <http://srab.cancer.gov/devcan>



# Estimated 5 year Survival Rates by Stage at Diagnosis

Five-year Relative Survival Rates\* (%) by Stage at Diagnosis, 1996-2004

Site	All Stages	Local	Regional	Distant	Site	All Stages	Local	Regional	Distant
Breast (female)	88.7	98.1	83.8	27.1	Ovary	45.5	92.7	71.1	30.6
Colon & rectum	64.4	89.7	68.4	10.8	Pancreas	5.1	20.0	8.2	1.8
Esophagus	15.8	34.4	17.1	2.8	Prostate <sup>§</sup>	98.9	100.0	—	31.7
Kidney <sup>†</sup>	66.5	89.9	61.3	9.9	Stomach	24.7	60.7	24.8	3.7
Larynx	62.5	80.9	50.2	23.4	Testis	95.5	99.3	95.7	71.1
Liver <sup>‡</sup>	11.7	23.8	7.7	2.9	Thyroid	96.9	99.7	96.9	57.8
Lung & bronchus	15.2	49.5	20.6	2.8	Urinary bladder	79.8	92.5	44.7	6.1
Melanoma of the skin	91.2	98.7	65.1	15.5	Uterine cervix	71.2	91.7	55.9	16.6
Oral cavity & pharynx	59.7	82.2	52.7	28.4	Uterine corpus	82.9	95.5	67.5	23.6

\* Rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 17 areas from 1996-2004, followed through 2005.

† Includes renal pelvis. ‡ Includes intrahepatic bile duct. § The rate for local stage represents local and regional stages combined.

**Local:** an invasive malignant cancer confined entirely to the organ of origin. **Regional:** a malignant cancer that 1) has extended beyond the limits of the organ of origin directly into surrounding organs or tissues; 2) involves regional lymph nodes by way of lymphatic system; or 3) has both regional extension and involvement of regional lymph nodes. **Distant:** a malignant cancer that has spread to parts of the body remote from the primary tumor either by direct extension or by discontinuous metastasis to distant organs, tissues, or via the lymphatic system to distant lymph nodes.

**Source:** Ries LAG, Melbert D, Krapcho M, et al. (eds). *SEER Cancer Statistics Review, 1975-2005*, National Cancer Institute, Bethesda, MD, [seer.cancer.gov/csr/1975\\_2005/](http://seer.cancer.gov/csr/1975_2005/), 2008.

American Cancer Society, Surveillance and Health Policy Research, 2009

# Imaging of Cancer Patients

## Pre-op Imaging

- Apply tumor biology principles
- What would change the type or timing your operation?

## Post-op Imaging

- Selective
- Patient anxiety
- Salvage surgery for recurrence is rare
- No prospective trial for “routine” post-op testing has shown a benefit in survival