Outline of Today’s Presentation

You are here

Time (years)

History of Cancer Surgery
Principles of Cancer Surgery

Outline

• The cancer problem
• Tumor staging
• Statistics and prediction tools
• Tumor biology
• Cancer molecules
• Things that make you say huh?
• New therapies for cancer patients
Integrating a Multidisciplinary Approach

- Surgical Oncology
- Medical Oncology
- Radiation Oncology
- Radiology
- Physical Therapy
- Pathology

Patient
## Magnitude of the Problem

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

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Estimated New Cases</th>
<th>Estimated Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Estimated New Cases</td>
<td>Estimated Deaths</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>192,280 (25%)</td>
<td>Lung &amp; bronchus</td>
<td>88,900 (30%)</td>
<td>Lung &amp; bronchus</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>116,090 (15%)</td>
<td>Prostate</td>
<td>27,360 (9%)</td>
<td>Prostate</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>75,590 (10%)</td>
<td>Colon &amp; rectum</td>
<td>25,240 (9%)</td>
<td>Colon &amp; rectum</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>52,810 (7%)</td>
<td>Uterine corpus</td>
<td>18,030 (6%)</td>
<td>Uterine corpus</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>39,080 (5%)</td>
<td>Non-Hodgkin lymphoma</td>
<td>12,590 (4%)</td>
<td>Melanoma of the skin</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>35,990 (5%)</td>
<td>Melanoma of the skin</td>
<td>9,830 (3%)</td>
<td>Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>35,430 (5%)</td>
<td>Thyroid</td>
<td>11,490 (4%)</td>
<td>Thyroid</td>
</tr>
<tr>
<td>Leukemia</td>
<td>25,630 (3%)</td>
<td>Kidney &amp; renal pelvis</td>
<td>10,180 (3%)</td>
<td>Kidney &amp; renal pelvis</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>25,240 (3%)</td>
<td>Ovary</td>
<td>9,670 (4%)</td>
<td>Liver &amp; intrahepatic bile duct</td>
</tr>
<tr>
<td>Pancreas</td>
<td>21,050 (3%)</td>
<td>Pancreas</td>
<td>7,780 (3%)</td>
<td>Pancreas</td>
</tr>
<tr>
<td>All sites</td>
<td>766,130 (100%)</td>
<td>All sites</td>
<td>6,070 (2%)</td>
<td>All sites</td>
</tr>
</tbody>
</table>

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

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www.cancer.org
The purpose of staging is to provide estimates of expected outcomes

- Facilitates treatment planning
- Allow comparisons between treatment groups

**American Joint Commission on Cancer (AJCC)**

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

**General Classification**

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

* The future of staging will lie in the molecular profile of tumor and host
Staging and Estimated 5 year Survival Rates at Diagnosis

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

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

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

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

- Median follow-up and survival
- Overall survival
- Relative differences vs. absolute differences
- Disease specific survival
- Disease free survival (recurrence free)
- Progression free survival

Guller U. JACS 2004;198:441-58
The probability of a cancer patient, who is alive 5 years after the original diagnosis, going on to survive another 5 years.

~ 90% for local disease
~ 85% for regional disease
~ 70% for distant disease
Prediction Tools - Melanoma

http://www.melanomaprosnosis.org/Predictiontools.aspx
Prediction Tools

Cancer Speak

Terms you have heard but may not know

- **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
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
Tumor Biology

Normal Epithelium → Hyper-proliferation → Early Adenoma → Intermediate Adenoma → Late Adenoma → Cancer

- APC loss
- K-ras mutation
- Chrom 18 loss
- p53 loss
What Does it Take to Make a Tumor?

- All tumors have multiple mutations
- Estimated to take at least 10 years from forming a cancer cell to metastasis
- Some mutations are critical for abnormal growth
  - Leukemia – BCR-ABL
  - GIST – cKit
- For most tumors, we haven’t found a dominant mutation
- Most mutations are believed to be “passengers”
What Does it Take to Make a Tumor?

- Sequenced the genome of 7 pancreatic tumors and their metastasis
- Classified as Founder and Progressor mutations
- Created evolutionary map
Epithelial to Mesenchymal Transformation (EMT)

Ponder this:

- Much of any tumor mass is stroma (i.e. not cancer epithelium)
  - Fibroblasts, extracellular matrix, myofibroblasts, blood vessels, immune cells
- In tumor xenograft models (human tumor grown in immune deficient mice)
  - Much of the stroma is of mouse origin
- In bone marrow transplant patients who receive bone marrow from the opposite sex and develop CR, Breast, or Gastric cancer
  - Tumor cells are from the host
  - Stroma cells are from the donor!

Understanding tumor biology is critical for:
• deciding when to operate
• deciding what operation to do
• deciding when NOT to operate
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
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

<table>
<thead>
<tr>
<th>Disease</th>
<th>Marker</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAP</td>
<td>APC</td>
<td>Colectomy</td>
</tr>
<tr>
<td>MEN 2</td>
<td>RET</td>
<td>Thyroidectomy</td>
</tr>
<tr>
<td>Familial Breast Cancer</td>
<td>BRCA 1,2</td>
<td>Mastectomy</td>
</tr>
<tr>
<td>Familial Ovarian Cancer</td>
<td>?</td>
<td>Oophorectomy</td>
</tr>
</tbody>
</table>
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 is problematic at best
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
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
- Therefore the assessment of lymph nodes is a prognostic tool
  (that will one day be supplanted by molecular tools)
Principles of Palliative Surgery

• One cannot palliate asymptomatic cancer patients
• Address the highest priority symptom first
• Manage expectations
• 25% will fail immediately
• 25% will recur with same symptom
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
- Tumors with a mutation in KRAS (downstream of EGRF) do not respond to EGFR receptor blockade
- Tumor analysis now required to treat with these agents
Microsatellite Instability Pathway

Microsatellite Instability- DNA Mismatch Repair- Lynch Syndrome (HNPCC)

TGFβRII, IGF2R, Caspase 5, Bax, hMSH3/6, Others

Failure of MMR

Normal Epithelium  Abnormal Epithelium  Early Adenoma  Advanced Adenoma  Adenocarcinoma

Diploid
Characteristic
Histology
Microsatellite Unstable

Meta analysis of Death- MSI-H vs. MSS

Microsatellite Unstable CRCs May Not Respond to Adjuvant Chemotherapy

Ribic et al. NEJM 2003
Molecular Diagnostics

**Oncotype Dx for Breast Cancer**

- 21 Gene PCR on fixed tissue
- Quantifies the likelihood of disease recurrence in early-stage breast cancer
- Assesses the likely benefit from certain types of chemotherapy

Paik S. J Clin Oncol. 2006;24(23):3726-34
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
Issues of Molecular Marker Detection

Immunohistochemical (IHC) = antibody based assessment
- Quick and easily adopted by most labs
- Strength of staining graded by the pathologist
- Examples - Breast – ER/PR, HER2/neu, and GIST – CD117

Polymerase Chain Reaction (PCR) = Gene or mutation present
- Certified lab
- Takes days to weeks for results
- Examples – Colon cancer KRAS, Melanoma BRAF
New Immune Therapies

Sipuleucel-T (Provenge)

- FDA approved April 2010 for hormone resistant metastatic prostate cancer
- First therapeutic cancer vaccine to improve overall survival in Phase III trials
- Improved median survival from 21 to 25 months ($93,000)

- Extract antigen presenting cells (dendritic cells) from patient
- Mix with prostatic acid phosphatase (PAP)
- Stimulate with GM-CSF
- Re-infuse to patient three times, two weeks apart

New Immune Therapies

Anti CTLA-4 antibody (Ipilimumab)

- Cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4) is an immune checkpoint molecule that down-regulates pathways of T-cell activation
  - HLA-A2 patients with metastatic disease progressing on therapy
  - Randomized to Ipilimumab +/- gp100 vaccine
  - Improved overall survival from 6 to 10 months
  - Autoimmune major toxicity in 10-15%

New Targeted Therapies

BRAF inhibitor in Melanoma - PLX4032

• BRAF (V600E) mutation present in about 50% of melanoma
• BRAF mutation activates MAP Kinase pathway
• In phase I trial 26 out of 32 metastatic patients responded
• Phase III trial ongoing

New Targeted Therapies

Hedgehog Pathway Inhibitors

- Hedgehog signaling pathway important in embryogenesis
- Regulating adult stem cells
- Involved in maintenance and regeneration of adult tissues

- Metastatic basal cell carcinoma refractory to conventional chemotherapy
- Frequently associated with mutations in hedgehog signaling pathway
- GDC-0449 an inhibitor of smoothened homologue (SMO) of hedgehog
- Phase I trial in which 18/33 patients had a measureable response

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
Lynch Syndrome Results From Failure of DNA Mismatch Repair (MMR) Genes

Base pair mismatch

Normal DNA repair

Defective DNA repair (MMR+)

MLH-1, MSH-2
MSH-6, PMS-2
Microsatellite Instability
PCR or IHC
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
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

Sarcoma

- 1-2 cm gross margin
- Preserve neurovascular structures
- No need for lymph nodes*
- Radiation reduces local recurrence
- Chemotherapy of limited value
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 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
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
?
<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Estimated Tumor Doubling Time (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choriocarcinoma</td>
<td>1.5</td>
</tr>
<tr>
<td>ALL</td>
<td>4-6</td>
</tr>
<tr>
<td>Hodgkin’s</td>
<td>38</td>
</tr>
<tr>
<td>GI adenocarcinoma</td>
<td>80-130</td>
</tr>
</tbody>
</table>

Scope of the Problem

Estimated number of new cancer cases for 2008, excluding basal and squamous cell skin cancers and in situ carcinomas except uterine bladder.

Notes: State estimates are offered as a rough guide and should be interpreted with caution. State estimates may not add to US total due to rounding.
Scope of the Problem


www.cancer.org
Scope of the Problem

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

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

www.cancer.org
Scope of the Problem


*Age-adjusted to the 2000 US standard population.
## Scope of the Problem

<table>
<thead>
<tr>
<th>2007 Estimated US Cancer Cases*</th>
<th>Men 766,860</th>
<th>Women 678,060</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>29%</td>
<td>26%</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>10%</td>
<td>11%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Kidney</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>All Other Sites</td>
<td>19%</td>
<td>21%</td>
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</table>

*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.
## Scope of the Problem

<table>
<thead>
<tr>
<th>Probability of Developing Invasive Cancers (%) Over Selected Age Intervals by Sex, US, 2003-2005*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 39</td>
</tr>
<tr>
<td>All sites†</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Urinary bladder†</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Breast</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
</tr>
<tr>
<td></td>
</tr>
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<td></td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Melanoma of the skin§</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Prostate</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Uterine cervix</td>
</tr>
</tbody>
</table>

*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.

Scope of the Problem

Cancer Incidence Rates*, All Sites Combined, All Races, 1975-2003

Rate Per 100,000

Men

Both Sexes

Women

*Age-adjusted to the 2000 US standard population and adjusted for delay in reporting.

www.cancer.org
# Scope of the Problem

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>50</td>
<td>53</td>
<td>66</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>75</td>
<td>79</td>
<td>89</td>
</tr>
<tr>
<td>Colon</td>
<td>51</td>
<td>59</td>
<td>65</td>
</tr>
<tr>
<td>Leukemia</td>
<td>35</td>
<td>42</td>
<td>49</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>13</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>Melanoma</td>
<td>82</td>
<td>86</td>
<td>92</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>48</td>
<td>53</td>
<td>63</td>
</tr>
<tr>
<td>Ovary</td>
<td>37</td>
<td>40</td>
<td>45(^1)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Prostate</td>
<td>69</td>
<td>76</td>
<td>100</td>
</tr>
<tr>
<td>Rectum</td>
<td>49</td>
<td>57</td>
<td>66</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>73</td>
<td>78</td>
<td>82</td>
</tr>
</tbody>
</table>

*Five-year relative survival rates based on follow up of patients through 2003.
\(^1\)Recent changes in classification of ovarian cancer have affected 1996-2002 survival rates.

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

<table>
<thead>
<tr>
<th>Score</th>
<th>1-yr</th>
<th>2-yr</th>
<th>3-yr</th>
<th>4-yr</th>
<th>5-yr</th>
<th>Median (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>93</td>
<td>79</td>
<td>72</td>
<td>60</td>
<td>60</td>
<td>74</td>
</tr>
<tr>
<td>1</td>
<td>91</td>
<td>76</td>
<td>66</td>
<td>54</td>
<td>44</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>89</td>
<td>73</td>
<td>60</td>
<td>51</td>
<td>40</td>
<td>47</td>
</tr>
<tr>
<td>3</td>
<td>86</td>
<td>67</td>
<td>42</td>
<td>25</td>
<td>20</td>
<td>33</td>
</tr>
<tr>
<td>4</td>
<td>70</td>
<td>45</td>
<td>38</td>
<td>29</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>71</td>
<td>45</td>
<td>27</td>
<td>14</td>
<td>14</td>
<td>22</td>
</tr>
</tbody>
</table>

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

Radical Surgery vs Time
## Scope of the Problem

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

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites†</td>
<td>1 in 3</td>
</tr>
<tr>
<td>Breast</td>
<td>1 in 8</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>1 in 16</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>1 in 19</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>1 in 40</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 55</td>
</tr>
<tr>
<td>Ovary</td>
<td>1 in 69</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1 in 73</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1 in 79</td>
</tr>
<tr>
<td>Urinary bladder‡</td>
<td>1 in 87</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>1 in 138</td>
</tr>
</tbody>
</table>

* 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.

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

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

* 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.

[www.cancer.org](http://www.cancer.org)
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
Note – add timeline scale of surgery -500 years experience condensed to 45 minutes
Yachida S. Nature 2010; Oct 28; 467(7319):1114-7
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
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