Update on Breast Cancer
Risk Factors, Prevention, Early Detection, and Treatment
(with Attention to High Risk Populations)

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October 24, 2013
Worldwide Epidemiology

• The incidence of breast cancer continues to rise 1.3 million patients each year

• Breast cancer accounts for 15% of all female deaths each year

• 2.6 million women alive with breast cancer in America today
### US Breast Cancer Statistics

1 in 8 Women will develop Breast Cancer

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>203,500</td>
<td>39,600</td>
</tr>
<tr>
<td>2003</td>
<td>211,300</td>
<td>40,580</td>
</tr>
<tr>
<td>2004</td>
<td>215,990</td>
<td>40,110</td>
</tr>
<tr>
<td>2005</td>
<td>211,240</td>
<td>40,410</td>
</tr>
<tr>
<td>2006</td>
<td>212,920</td>
<td>40,970</td>
</tr>
<tr>
<td>2007</td>
<td>178,480</td>
<td>40,460</td>
</tr>
<tr>
<td>2008</td>
<td>182,460</td>
<td>40,480</td>
</tr>
<tr>
<td>2009</td>
<td>192,370</td>
<td>40,170</td>
</tr>
<tr>
<td>2010</td>
<td>207,090</td>
<td>39,840</td>
</tr>
<tr>
<td>2011</td>
<td>230,480</td>
<td>39,520</td>
</tr>
<tr>
<td>2012</td>
<td>226,870</td>
<td>39,510</td>
</tr>
<tr>
<td>2013</td>
<td>232,340</td>
<td>39,620</td>
</tr>
</tbody>
</table>
Why The Increased Incidence?

- Women living longer
- Earlier detection
- More widespread availability of mammography
- Higher socioeconomic status
- ? Environmental factors
- ? Role of tobacco increasing the risk of premenopausal breast cancer (Lancet 2002)
## U.S. Survival Statistics
### Improving Survival Rates

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>50</td>
<td>54</td>
<td>68</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>75</td>
<td>79</td>
<td>90</td>
</tr>
<tr>
<td>Colon</td>
<td>52</td>
<td>59</td>
<td>66</td>
</tr>
<tr>
<td>Leukemia</td>
<td>36</td>
<td>42</td>
<td>55</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>13</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>Melanoma</td>
<td>83</td>
<td>87</td>
<td>93</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>48</td>
<td>53</td>
<td>69</td>
</tr>
<tr>
<td>Ovary</td>
<td>37</td>
<td>40</td>
<td>45</td>
</tr>
<tr>
<td>Pancreas</td>
<td>3</td>
<td>3</td>
<td>6</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>69</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>74</td>
<td>78</td>
<td>81</td>
</tr>
</tbody>
</table>

*5-year relative survival rates based on follow up of patients through 2007.
Source: Surveillance, Epidemiology, and End Results Program, 1975-2007, Division of Cancer Control and Population Sciences, National Cancer Institute, 2010.*
# U.S. Survival Statistics by Race

## Cancer Survival*(%) by Race, 1999-2006

<table>
<thead>
<tr>
<th>Site</th>
<th>White</th>
<th>African American</th>
<th>Absolute Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>67</td>
<td>58</td>
<td>9</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>90</td>
<td>78</td>
<td>12</td>
</tr>
<tr>
<td>Colon</td>
<td>65</td>
<td>56</td>
<td>9</td>
</tr>
<tr>
<td>Esophagus</td>
<td>18</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Leukemia</td>
<td>54</td>
<td>47</td>
<td>7</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>68</td>
<td>59</td>
<td>9</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>63</td>
<td>42</td>
<td>21</td>
</tr>
<tr>
<td>Prostate</td>
<td>100</td>
<td>96</td>
<td>4</td>
</tr>
<tr>
<td>Rectum</td>
<td>67</td>
<td>58</td>
<td>9</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>80</td>
<td>66</td>
<td>14</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>72</td>
<td>61</td>
<td>11</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>86</td>
<td>62</td>
<td>24</td>
</tr>
</tbody>
</table>

*5-year relative survival rates based on cancer patients diagnosed from 1999 to 2006 and followed through 2007.

Source: SEER 17 registries, Surveillance, Epidemiology, and End Results Program, Division of Cancer Control and Population Sciences, National Cancer Institute, 2010.
U.S. Survival Statistics

Mortality Rate Decreased 30% by 2013

<table>
<thead>
<tr>
<th>Stage</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>In situ</td>
<td>100%</td>
</tr>
<tr>
<td>Stage I</td>
<td>100%</td>
</tr>
<tr>
<td>Stage II</td>
<td>81-92%</td>
</tr>
<tr>
<td>Stage III</td>
<td>54-67%</td>
</tr>
<tr>
<td>Stage IV</td>
<td>20%</td>
</tr>
<tr>
<td>Year</td>
<td>Incidence</td>
</tr>
<tr>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td>2002</td>
<td>1,500</td>
</tr>
<tr>
<td>2003</td>
<td>1,300</td>
</tr>
<tr>
<td>2004</td>
<td>1,450</td>
</tr>
<tr>
<td>2005</td>
<td>1,690</td>
</tr>
<tr>
<td>2006</td>
<td>1,720</td>
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<tr>
<td>2007</td>
<td>2,030</td>
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<tr>
<td>2008</td>
<td>1,900</td>
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<tr>
<td>2009</td>
<td>1,910</td>
</tr>
<tr>
<td>2010</td>
<td>1,970</td>
</tr>
<tr>
<td>2011</td>
<td>2,140</td>
</tr>
<tr>
<td>2012</td>
<td>2,190</td>
</tr>
<tr>
<td>2013 Projected</td>
<td>2,400</td>
</tr>
</tbody>
</table>
Statistically Identified Risk Factors for Developing Breast Cancer

- Increased age
- Maternal first degree relative
- Pathological diagnosis of
  - Atypical hyperplasia
  - Lobular carcinoma In situ
- Menarche before 11 years old
- Menopause after 50 years old
- Nulliparity
- First birth after 30 years old
- History of contralateral breast cancer
Age and Breast Cancer Risk

Female Breast Cancer Incidence
SEER, 1988-92

Rate per 100,000

Age Group
Lifestyle Risk Factors for Developing Breast Cancer

- Alcohol—More than 3 alcoholic beverages/week
- Obesity
- Hormone Replacement Therapy – 1.4 x risk
- Oral Contraceptive use
- Tobacco use within 5 years of menarche
  - 70% increased risk of developing premenopausal breast cancer
- Too little exercise
- Diet – fat, red meat
Race and Breast Cancer Risk

• Race: (Black, White)
  – If age < 45, risk is slightly higher in black women
  – If age > 44, risk is substantially higher among white women
  – “Basal-like” triple negative cancers in black women
Breast Cancer is a Different Disease in Black Women

- Develops at a younger age
- More aggressive biologically
In Women Under 40 Years of Age

<table>
<thead>
<tr>
<th></th>
<th>Incidence</th>
<th>Age of Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>64 per 100,000</td>
<td>35% before Age 50</td>
</tr>
<tr>
<td>White</td>
<td>57 per 100,000</td>
<td>20% before Age 50</td>
</tr>
</tbody>
</table>

Cancer 2002; 95:21-7
Earlier age of onset in Black Women may contribute to delay in diagnosis

<table>
<thead>
<tr>
<th>Age</th>
<th>Black women’s incidence of breast cancer compared to white women</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 – 29 years</td>
<td>1.5 fold increase</td>
</tr>
<tr>
<td>30 – 34 years</td>
<td>1.3 fold increase</td>
</tr>
</tbody>
</table>

Breast Cancer Characteristics

• In Black Women breast cancer presents with:
  – More aggressive disease
  – Higher grade
  – Negative estrogen and progesterone receptor status
  – Shorter disease free survival

• Issues
  – Few clues to help identify these early onset cases
  – Requires a heightened awareness of susceptible women
  – Must target screenings and interventions to detect the cancer
  and treat these women earlier

Cancer Res 2006; 66(17): 8327-30
Black and Hispanic Women

- Tumors among Black and Hispanic Women are more likely:
  - To be > 2cm at time of diagnosis
  - To be lymph node positive
  - To be estrogen neg and progesterone neg
  - To be poorly differentiated

Mortality Rate

• Black women mortality rate is 37% higher (across all age groups)

**Despite**

• White women having substantially higher incidence rates

• Exception: Black women < 35 years old have higher incidence

Ca Cancer J Clin 2006;56: 168-83
Mortality Rate

• Overall age adjusted mortality rates are higher among Afro-American women than white women by **1.5 - 2.2 fold**

• First noted in mid-1970s and continues to increase

Cancer 2007; 110: 1880-8
Why Are There Disparities?

- Inequalities in access to care is a major factor but not the **only** factor.

- US Dept of Defense Health Care System showed that black women treated at no cost and with equal access to care had worse overall survival.

- Therefore, biological processes are important to recognize.

Cancer 2003; 98, Nov 5th
Cancer 2007; 110: 1880-8
Biological Processes

• Obesity and diet?
  – Increased levels of circulating estrogens

• Response to systemic adjuvant therapy
  – Poorly differentiated, basal, triple negative (ER neg, PR neg, Her Neu2 neg) tumors do not respond as well to treatment
  – These are seen more frequently in Afro-American women

• Racial bias
  – Different treatment
  – Initial treatment delays
  – Failure to give adjuvant treatment
What Can We Do As Clinicians?

• Be cognizant of statistics in young black women
  – Breast cancer develops at a younger age
  – Breast cancer is more aggressive

• Thorough history taking
  – Thorough breast status and history
  – Thorough family history of breast and ovarian cancer

• Thorough physical examination

• Individualize each patient's work-up based on her symptoms, physical findings and increased risk base on ethnicity
  – Don’t let a negative family history sway your decision for further diagnostic tests
  – Reconsider the “standard” recommendations for baseline mammogram at the age of 40 (which is based on statistics of white women)
How Else Can A Health Care Provider Help?

• Advocate for:
  – Policy change for more equitable access to health care for all Americans
  
  – Research to better understand the biology of aggressive breast cancer in Afro-American women so we can develop better guidelines for screening to detect breast cancer earlier

  – Research to elucidate the character of triple negative, basal cancers to find more effective treatments
But Most Important!

- When you see a young black woman think about the possibility of breast cancer until proven otherwise
- Take her and her family’s history
- Do a thorough examination
- Think twice: should she have a mammogram or ultrasound?
However, clinical research in population studies has shown definite strategies that, if followed, especially in youth, can decrease the possibility of developing breast cancer.
Prevention
How Can Breast Cancer Be Prevented?
To Prevent Cancer, We Must Understand What Causes Cancer

• In lung cancer this is simple – tobacco

• Breast & prostate cancer are not so simple
  The cause is multifactorial for each
Prevention

• Chemo prevention

• Is there a protective benefit from exercise and dietary practices?

Tamoxifen

- A drug which can prevent breast cancer
STAR Trial Results

• Raloxifene- An additional tool to prevent breast cancer in post menopausal women

• Aromatase Inhibitors – in post menopausal women
Breast Cancer Prevention:

• Additional Strategies

• How women themselves can play an active role.
Breast Cancer

- Prevention strategies should be directed primarily at girls and young women
  - Maintain ideal body weight
  - Participate in sports
- Especially before puberty
Obesity

• Obesity increases your risk of developing Breast Cancer in America

• 1 in 10 children are obese

• Obesity increased 61% from 1991 – 2000

• 19.2 million American women are obese
Physical inactivity, obesity and poor nutrition together kill just more than 45 people each hour

16.6% of total U.S. deaths

400,000 deaths per year

JAMA 2004;291:1238-45
• Evidence from 15 clinical studies have shown a decreased risk of developing breast cancer in physically active women.

Exercise

• A conclusive study, published in the “New England Journal of Medicine” in 1997, confirmed these findings.
Pre and Postmenopausal Women

Exercise at least 4 hours per week

A 37% lower risk of developing breast cancer
Dietary Practices and Breast Cancer Prevention
Limit Alcohol

Updated recommendations from 2012 Dana Farber study:

More than 3 alcoholic beverages per week increases the risk of developing breast cancer.
Relationship Between Daily Alcohol Use and Risk of Breast Cancer

![Graph showing the relationship between alcohol consumption and breast cancer risk. The x-axis represents alcohol consumed (g/d), ranging from 0 to 36. The y-axis represents relative risk, ranging from 0 to 3. The graph indicates an increase in relative risk with higher alcohol consumption.]
Does fat intake influence the development of breast cancer?

- Studies suggest quantity does not play a role.

But

- Maybe the type of fat plays a role. Olive oil shows a benefit in Mediterranean studies.
Dietary Fat’s Relationship with Breast Cancer

- No association between dietary fat and breast cancer risk. (Lancet July 2003)

- High polyunsaturated fatty acid ratio in diet may reduce the risk of breast cancer. (Journal of Nutrition, May 2003)
What about Meats & Fish?

1. Conflicting studies on the role of a diet high in red meat increasing the risk of breast cancer

2. BUT, studies clearly show a benefit from a diet high in fish intake.
• Red meat intake associated with increased breast cancer risk.

• Fish and dairy product intake associated with decreased breast cancer risk.

(Cancer Causes Control, Feb 2003)
Soy Products

- Are these beneficial?
- Why?
- Which forms?
- What daily intake is beneficial?

Phyto estrogens – also found in flax seeds
Soy Product & Breast Cancer

• In Japan, in Asian women in general and in Asian American women – High soy intake is associated with a decreased risk of breast cancer.

(J of the National Cancer Institute, June 2003)
(Carcinogenesis, September 2003)
• However, case control studies and studies in Asian-American women have shown that high intake in childhood and adolescence may decrease the risk of developing breast cancer.

• Therefore, age of consumption may be the key as to whether soy intake exerts a protective role against developing breast cancer.

(Carcinogenesis, September 2002)
Does Smoking Cause Breast Cancer?
Does Smoking Cause Breast Cancer?

Previous studies have said no, except:

• In women with a strong family history of breast cancer, smoking increases the risk of developing breast cancer even more

  And

• Australian studies are looking at the effect of second hand smoke on teenage girls causing an increased risk of developing breast cancer.
Experimental evidence shows chemicals in tobacco smoke induced cancerous transformation of human breast cells.
Human breast tissue is most sensitive to environmental carcinogens during periods of rapid cell growth

*During puberty
*In women never having children

(Lancet, October 2002)
A New Study Has Shown:

- A 70% increased risk of developing premenopausal breast cancer if young women start smoking in their teens within 5 years of their first period.

- 30% of high school senior girls smoke in the US – a large increase in the risk of developing breast cancer.

- In women never having had children if they have smoked 20 cigarettes per day for 20 years – increased risk.
Does Low-Dose Aspirin Prevent Breast Cancer?

Diagnosis
Diagnostic Imaging

- Mammography
- Sestamibi Scans
- Ultrasound
- MRI
- Tomosynthesis
- PET Scans
Limitations of Mammography

- 7-10% False negative role
- Sensitivity decreases when breast tissue is dense
- 40-50% of women <50 years old have dense breasts
Digital Mammogram

- Technique is same as conventional; image presented on high resolution computer screen

- Enables manipulation of contrast, density magnification, orientation adjusted to optimize reporting conditions

  Sensitivity: digital = film
  Specificity: digital = film

Digital mammography is superior to film mammography in detecting breast cancer but only in women under 50 yrs.

- NEJM 353:1773-83, 2005
Computer Assisted Detection Mammogram (CAD)

- Has not be shown to be superior to standard reading of mammograms in the detection of cancer

*Journal of the National Cancer Institute* 2004; 96:162-63, 185-190 February 4, 2004
Nuclear Medicine Scan:  
**Sestamibi**

- Used as an adjunct to mammography in dense or multiple-biopsied, difficult to assess breasts
Ultrasound Evaluation of the Breast

To evaluate nodular densities for:
1. Cystic vs solid character
2. Contour & texture characteristics
3. Size
4. Vascularity

???? Should it be a screening tool itself???
AN ACT REQUIRING COMMUNICATION OF MAMMOGRAPHIC BREAST DENSITY INFORMATION TO PATIENTS.

Be it enacted by the Senate and House of Representatives in General Assembly convened:

Section 1. Section 38a-503 of the general statutes is repealed and the following is substituted in lieu thereof (Effective October 1, 2009):

(a) Each individual health insurance policy providing coverage of the type specified in subdivisions (1), (2), (4), (6), (10), (11) and (12) of section 38a-469 delivered, issued for delivery, renewed, amended or continued in this state on or after October 1, 2001, shall provide benefits for mammographic examinations to any woman covered under the policy which are at least equal to the following minimum requirements: (1) A baseline mammogram for any woman who is thirty-five to thirty-nine years of age, inclusive; and (2) a mammogram every year for any woman who is forty years of age or older. Such policy shall provide additional benefits for comprehensive ultrasound screening of an entire breast or breasts if a mammogram demonstrates heterogeneous or dense breast tissue based on the Breast Imaging Reporting and Data System established by the American College of Radiology or if a woman is believed to be at increased risk for breast cancer due to family history or prior personal history of breast cancer, positive genetic testing or other indications as determined by a woman's physician or advanced practice registered nurse.

(b) Benefits under this section shall be subject to any policy provisions that apply to other services covered by such policy.
Breast US as Screening Tool

- Until April 2009, no scientific support for using ultrasound as a screening tool

- American College of Radiology Imaging Network (ACRIN)
  - Seven single center studies
  - Two multi-center trials

- Women at very high risk who cannot tolerate MRI
- Women at intermediate of breast cancer
  - Have a personal history of breast cancer
  - Prior LCIS
  - Prior Atypical Hyperplasia
  - Intermediate family history with dense parenchyma
  - All women with dense breasts
Benefits of MRI

In some cases:

- Attractive option to identify lesions that evade detection otherwise
- Role in evaluating disease extent
- Good at screening high risk patients
- Several studies show:
  - Sensitivity 86-100% > wide range
  - Specificity 37-97% > wide range
Limitations of MRI

• Enhanced visualization during proliferative phase of menstrual cycle i.e., an MRI the week before menses onset is a very different image than one week after

• Excessively high false positives (+), resulting in specificity < 40%

• False results can lead to unnecessary surgery

• Unable to distinguish normal from carcinomatous enhancement of nipple

• Insurance coverage issues
What Role Does MRI Have in Breast Care?

In women with diagnosed breast cancer:

1. To determine extent of cancer to guide breast conservation

2. To evaluate for multi-centric disease

3. To assess the contralateral breast if otherwise difficult to evaluate
Two studies confirm a definite role for MRI in surveillance of women at high risk of developing breast cancer in:

- Carriers of the BRCA1 and BRCA2 mutation

- Women with a familial predisposition (strong family history of breast cancer)

New England Journal of Medicine, 351(5) July 29, 2004
JAMA, 292 (11) September 15, 2004
CA for Clinicians, 57(2),75-87, March 2007
With further refinement, MRI has the potential for:

- Diagnosing occult breast cancer
- Estimating tumor margins, aiding localization
- Defining extent, multi focality; aid in breast conserving therapy
- Success depends on:
  - Quality of Image
  - Interpretation
  - Availability
  - Skillful Management
MRI

However, MRIs can miss extensive DCIS, yet can vastly over read the extent of invasive disease leading to a need for tissue diagnosis.
Researchers at the Mayo Clinic investigated the relationship between mastectomy rates and the use of preoperative magnetic resonance imaging (MRI). The study included nearly 5,500 breast cancer patients who had undergone surgery at Mayo Clinic between 1997 and 2006. The researchers found that mastectomy rates decreased from 1997 to 2003 but increased from 2004 to 2006, rising to levels seen a decade earlier. Patients who had a preoperative MRI were more likely than those who had not to undergo a mastectomy.

Citation: R. Katipamula, et al. J Clin Oncol 26: 2008 (May 20 suppl: abstr 509)
http://www.asco.org/ASCO/Abstracts%3B%26%2BVirtual%26Meeting/Abstracts?&vmview=abst_detail_view&confID=55&abstractID=30991
© Oxford University Press 2008. DOI: 10.1093/jnci/djn273

Ultrasound and MRI Screening Guidelines

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<tr>
<th>MRI</th>
<th>Known BRCA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First degree relative of known BRCA, untested</td>
</tr>
<tr>
<td></td>
<td>Lifetime risk &gt; 20%</td>
</tr>
<tr>
<td></td>
<td>Other generic syndromes and first degree relatives</td>
</tr>
<tr>
<td></td>
<td>(Li-Fraumeni, Cowden, Bannayan-Riley-Ruvalcaba)</td>
</tr>
<tr>
<td></td>
<td>Radiation therapy to chest between age 10-30</td>
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</tbody>
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<table>
<thead>
<tr>
<th>ULTRASOUND</th>
<th>High risk patient who can’t have or tolerate MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women with dense breasts who aren’t approved for MRI</td>
</tr>
<tr>
<td></td>
<td>Mentally unable to have mammograms</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INTERMEDIATE RISK PATIENTS</th>
<th>Those with personal history of breast cancer, lobular neoplasia or ADH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prefer to have screening MRI if they can be approved, but would defer to screening ultrasound if not approved</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MAMMOGRAPHY</th>
<th>Baseline between age 35-40, yearly after age 40</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BRCA1, start by age 25</td>
</tr>
<tr>
<td></td>
<td>BRCA2, start between age 25-30</td>
</tr>
<tr>
<td></td>
<td>Chest radiation (&gt;20Gy), start 8 years after radiation or age 25, whichever is later</td>
</tr>
<tr>
<td></td>
<td>First degree relative with breast cancer, start 10 years before age of onset, but on &lt;30 unless suspect BRCA</td>
</tr>
<tr>
<td></td>
<td>Annually after personal history of breast cancer, any age</td>
</tr>
</tbody>
</table>
Value of MRI in BRCA Positive Patients

- Survival of BRCA positive patients is equivalent in patients screened with annual MRIs versus prophylactic mastectomies

JCO 2010
• Tomoynthysis
  – ?Superior to digital mammograms
  – ? of radiation dose
  – Sensitivity/specificity
  – Prospective data will answer these questions
PET SCAN
PET Scan - Indications

1. FDA Approved for Evaluation of **Metastatic Disease** in Breast Cancer patients

2. **Recent studies show**: Pet Scans have a high rate of detecting axillary lymph node metastases with low false negatives, as well as identifying other positive nodes not accessible to surgery (e.g., supra clavicular nodes, internal mammary chain)
PET Staging of Axilla

1. A positive PET scan is highly accurate.

2. However, a negative PET does not accurately reflect nodal disease.

Making the Diagnosis

Breast Cancer

1. Palpable Masses
   - Fine needle aspiration biopsy
   - Core biopsy
   - Surgical biopsy

2. Non palpable abnormalities
   - Ultrasound-guided core biopsy
   - Stereotactic or mammotome core biopsy
   - Ultrasound or mammographically placed needle localization for surgical excision
   - Advanced Breast Biopsy Instrumentation (ABBI)
Ultrasound-Guided Core Biopsy and Stereotactic/Mammotome Core Biopsy

- 99% Accurate
- 0 % infection rate
- 0-1 % hematoma Rate
- Minimal skin scarring
- No deformity
- Must have 6 month follow up diagnostic study and physical exam
Serum Markers for Breast Cancer

- CEA
- CA 15.3
- Are not standard reliable markers for follow up
- Should only be used in the context of a clinical trial
Onco Type – DX
Microarray Analysis of Tumor Genes

• Revolutionary tool

• To help customize the treatment of women with breast cancer diagnosed

• ER+ tumors that are node negative
Can BRCA help decide breast conservation versus mastectomies?
Can BRCA help decide......

• Memorial Sloan Kettering meta-analysis study shows equal local recurrence rate and survival for women with BRCA 1 or 2 mutations with breast conservation or mastectomy ---- The same as the general population.
• **Summary of Recommendations**

• The U.S. Preventive Services Task Force (USPSTF) recommends against routine referral for genetic counseling or routine breast cancer susceptibility gene (*BRCA*) testing for women whose family history is not associated with an increased risk for deleterious mutations in breast cancer susceptibility gene 1 (*BRCA1*) or breast cancer susceptibility gene 2 (*BRCA2*).

• The USPSTF recommends that women whose family history is associated with an increased risk for deleterious mutations in *BRCA1* or *BRCA2* genes be referred for genetic counseling and evaluation for BRCA testing.
### HEREDITARY BREAST AND/OR OVARIAN CANCER SYNDROME TESTING CRITERIA\(^a,b,c\)

- Individual from a family with a known deleterious BRCA1/BRCA2 mutation
- Personal history of breast cancer\(^d\) + one or more of the following:
  - Diagnosed age ≤ 45 y
  - Diagnosed age ≤ 50 y with ≥ 1 close blood relative\(^e\) with breast cancer ≤ 50 y and/or ≥ 1 close blood relative\(^e\) with epithelial ovarian/fallopian tube/primary peritoneal cancer at any age
  - Two breast primaries\(^f\) when first breast cancer diagnosis occurred prior to age 50 y
  - Diagnosed age < 60 y with a triple negative breast cancer
  - Diagnosed age < 50 y with a limited family history\(^c\)
  - Diagnosed at any age, with ≥ 2 close blood relatives\(^e\) with breast and/or epithelial ovarian/fallopian tube/primary peritoneal cancer at any age
  - Close male blood relative\(^\text{g}\) with breast cancer
  - Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer
  - For an individual of ethnicity associated with higher mutation frequency (eg, Ashkenazi Jewish) no additional family history may be required\(^h\)

- Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer
- Personal history of male breast cancer
- Personal history of breast and/or ovarian cancer at any age with ≥ 2 close blood relatives\(^e\) with pancreatic cancer at any age
- Personal history of pancreatic cancer at any age with ≥ 2 close blood relatives\(^e\) with breast and/or ovarian and/or pancreatic cancer at any age

#### HBOC criteria met
- See Follow-up (HBOC-2)

#### HBOC criteria not met
- See NCCN Breast Cancer Screening and Diagnosis Guidelines

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\(^a\)One or more of these criteria is suggestive of hereditary breast/ovarian cancer syndrome that warrants further professional evaluation. The maternal and paternal sides should be considered independently. Other malignancies reported in some HBOC families include prostate and melanoma.

\(^b\)Patients who have received an allogeneic bone marrow transplant should not have molecular genetic testing via blood or buccal samples due to contamination by donor DNA. DNA should be extracted from a fibroblast culture.

\(^c\)Individuals with limited family history, such as fewer than 2 first- or second-degree female relatives or female relatives surviving beyond 45 years in either lineage, may have an underestimated probability of a familial mutation.

\(^d\)For the purposes of these guidelines, invasive and ductal carcinoma in situ breast cancers should be included.

\(^e\)Close blood relatives include first-, second-, and third-degree relatives.

\(^f\)Two breast primaries including bilateral disease or cases where there are two or more clearly separate ipsilateral primary tumors.

\(^g\)Ovarian cancer is a component tumor of hereditary non-polyposis colorectal cancer/Lynch syndrome, be attentive for clinical evidence of this syndrome.

\(^h\)Testing for Ashkenazi Jewish founder-specific mutation(s), should be performed first. Full sequencing may be considered if ancestry also includes non-Ashkenazi Jewish relatives or other HBOC criteria is met. Founder mutations exist in other populations.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
NCCN Guidelines
Criteria for HBOC genetic testing

Patient with any of the following:
• Breast Cancer diagnosed age ≤45y
• Epithelial ovarian/fallopian/primary peritoneal cancer at any age
• Breast and Ovarian cancer at any age
• Male Breast Cancer at any age
• *Triple Negative breast cancer* <60y
NCCN Guidelines
Criteria for HBOC genetic testing

Personal history of breast cancer and:

• Diagnosed age <50y
  + limited family structure
  + 2\textsuperscript{nd} primary breast cancer at any age

• Diagnosed age ≤50y,
  + ≥ 1 close blood relative with breast cancer ≤ 50y,
    or
  + ≥ 1 close blood relative with epithelial ovarian/
    fallopian/primary peritoneal cancer at any age
NCCN Guidelines
Criteria for HBOC genetic testing

Breast Cancer at any age
+ ≥ 2 close blood relative with breast cancer and/or epithelial ovarian/fallopian/primary peritoneal cancer at any age, or
+ ≥ 1 close blood relative with male breast cancer, or
+ Jewish (Ashkenazi) ancestry

Breast and/or Ovarian Cancer at any age
+ ≥ 2 close blood relatives with pancreatic cancer

Pancreatic Cancer at any age
+ ≥ 2 close blood relatives with breast/ovarian/pancreatic cancer
NCCN Guidelines
Criteria for HBOC genetic testing

No personal history of cancer:

+ 1\textsuperscript{st} or 2\textsuperscript{nd} degree relative meets any of the previously mentioned criteria

+ known deleterious mutation in family
NCCN Guidelines
Criteria for Cancer Genetics Evaluation

• Breast cancer with a FHx of any of the following:
  – Thyroid cancer, especially follicular (PTEN)
  – Adrenocortical carcinoma (TP53)
  – Endometrial cancer (PTEN, ?Lynch)
  – Pancreatic Cancer (BRCA2, PALB2, p16)
  – Brain tumors (TP53, PTEN)
  – Diffuse gastric cancer (CDH1), especially with lobular breast cancer
  – Dermatologic findings associated with PTEN
NCCN Guidelines

Breast Cancer in Older Women
Age and Breast Cancer Risk

Female Breast Cancer Incidence
SEER, 1988-92

Rate per 100,000

Age Group
Age and Breast Cancer Risk

• Age is a significant risk factor for developing breast cancer

• The highest risk group are women aged 70 – 85 years
• 40% of breast cancers are diagnosed in Women aged > 65

SEER Database, June 6, 2010
Yet, the

- US Preventive Task Force (2009) and a study from Yale University (2012) recommends no screening mammograms be performed after age 70 yo, ignoring the highest risk group for developing breast cancer
• While the biology of breast cancer may be more favorable in older women with hormone receptor positive tumors

  – Presentation is often at a later stage (because of lack of screening), requiring more intrusive intervention. (Lancet Oncol. 2007; 8)

  – Approximately 20% of women > 70 yo have more biologically aggressive tumors that are larger and have nodal invasion. (Crit Rev Oncol. Hematol. 2008:67)
• Mammography has a much higher positive predictive value of an abnormality in older women who tend to have less dense breasts
• Ca Cancer J. Clin 2003; 53
To Screen or Not to Screen?

Therefore, the question arises:

• Should women over 70 yo have screening mammograms?
The Goal of Surgery

- From the Surgical perspective, the less surgery I need to do in a woman over age 70 yo that gives her the best chance of quality of life AND equivalent survival and local recurrence, balanced with her individual overall health status and the risks of the intervention is the GOAL.

- Therefore, the earlier and smaller the cancers are, the better for each woman.

- This requires very careful individualized care with strong family and support system input.
• For those making the decisions:

• The Issue is Cost Benefit Analysis
Some patient examples for you to consider...
Patient #1

- 82 yo woman, past history of colon cancer in remission x 5 years, followed by an oncologist. No mammograms ordered since diagnosis, ? of clinical breast exam
- PMH: Atrial Fibrillation, HTN, CHF
- Medicare investment in medications: $370/month; $4,440/year
- Beta-Blocker $50/mon, Pradoxa $320/mon, HCTZ - $ 5/mon
- SH: Married, very active cooking for extended family, summers at the shore, drives
- P.E: right breast - palpable 8 cm mass; Left - no masses
- Mammogram: Right mass - 8cm; Left: 1 cm mass - both invasive ductal cancer
- Course: patient required mastectomy on the right, requested bilateral mastectomies. Converted to Coumadin, then heparin perioperative, then Coumadin
- Surgery: 200 minutes Hospitalized: 8 days - $260,000
- Postop course prolonged due to systemic fluid issues and multiple drains. 4 months - no charge to Medicare.
- Bottom line: Bilateral mastectomies, and 4 month course of interference in quality of life
Patient #2

- 74 yo woman with nonpalpable 3 mm mammographic lesion; followed with 6 month mammogram which showed growth to 6 mm.
- PMH: CAD, HTN, CHF, H/O 3 TIAs, atrial fib
- Medicare investment in medications $435/month; $5220/year
- Levothyroxine $20/mon; Propanolol $50/mon; Tikosyn $300/mon; Coumadin $65/mon
- SH: widowed, lives alone independently, supportive daughter, drives, very active, oversees senior affairs commission in her town
- Results: Stereotactic biopsy: invasive ductal carcinoma
- Course: Patient required conversion to heparin perioperative, then Coumadin postop
- Treatment: Lumpectomy and excision of sentinel lymph node
- Surgery time: 75 minutes  Hospitalization: 5 days - $50,500
- Postop course: Postoperative swelling and bruising requiring no intervention and no pain medication
• Investment cost of annual screening mammogram

$88.80/year (Medicare)
• The decision is yours in communication with each patient based on individualized care
International Society of Geriatric Oncology recommends:

- A geriatric assessment which includes:
  - Co-morbidities - competing causes of mortality
  - Cognitive and functional status
  - Social situation - support system
  - Patient preferences
  - Barriers to treatment

Lancet Oncology 13(4); e148, 2012 Apr
In Conclusion

- A simple view, based on a quarter of a century of observation is this:
  - If a woman lives into her 70-80s and is active and functioning independently without memory issues and with her other health issues controlled by medication
  - Her life expectancy is likely to remain good......

- It is not reasonable to watch these very vital, fully living women suffer with advanced breast cancer, because of delay in diagnosis, as the final chapter to accelerating their end of life in a painful and incapacitating manner which is never swift nor easy.
• A large return: Early Detection with minimal surgery, minimal disruption of quality of life, and minimal disruption of the delicate balance of an older woman's total health

• For investment of: $ 88.80/year - Mammogram

• For investment of: $0 an annual clinical breast exam - Priceless

• As primary care physicians, you can make this difference.