Breast Cancer in the 21st Century

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Epidemiology

• In the United States Breast Cancer is:
  – The most common malignancy in women.
  – The second leading cause of cancer death.
  – The most common cause of death in women ages 40-59.
  – Annually about 200,000 women are affected and 40,000 die of advanced disease
  – Average age at diagnosis is 61
NCCN GUIDELINES
Breast Cancer Screening – Average Risk

• Age 20-39
  – Clinical breast exam
  – SBE encouraged
  – Imaging ONLY if symptoms

• Age > 40
  – Yearly breast exam
  – Annual mammography
  – SBE encouraged
  – No good data to discontinue screening
  – Decisions in elderly breast cancer are based on life expectancy and co-morbidities.
Breast Cancer Screening
HIGH RISK (NCCN guidelines)

- NCCN Guidelines for women age > 25
  - Annual mammogram
    - Start age 25 for genetic predisposition
    - Start 5-10 years prior to the youngest family member diagnosed with breast cancer if strong FH
    - Complete Breast Exam every 6-12 months
    - Breast MRI if strong family history or if radiation therapy for mediastinal Hodgkins Disease
    - Consider other therapies (mastectomy, chemoprevention)
U.S. Preventive Services Task Force

• The USPSTF is an independent panel of primary care physicians funded and staffed by the HHS. Medicare gave HHS authority to consider USPSTF recommendations in Medicare coverage determinations. Not one cancer care provider was on this panel.
USPSTF Recommendations

• Advise against mammography for women 40-49 years of age

• Provide mammograms only every other year for women between 50 and 74

• Stop all breast cancer screening in women over 74.
USPSTF recommendations

• These recommendations ignore the valid scientific data that since the onset of regular mammography, the mortality rate from breast cancer has decreased.
• Recommendations were based on computer models
• No breast cancer physician (radiologist, surgeon, medical or radiation oncologist) was included on the task force.
Mammography – remains the “Gold Standard”

• Not a perfect test but has been shown to save lives including in women ages 40-49.

• Since the onset of routine mammography the mortality from breast cancer has decreased by 30%

• Several trials have shown that screening reduces breast cancer mortality in women ages 50-74 by 26%.
Adjuncts to mammography

- Breast ultrasound – helps identify lesions as solid or cystic, malignant or benign appearing
- Breast MRI
  - More sensitive in HIGH RISK PATIENTS
  - NOT a screening tool, does have false +
  - Useful to image dense breasts
  - No association with improved survival
Screening Breast MRI

- No studies of the effects of screening breast MRI on breast cancer mortality have been published.
- Screening MRI is recommended for women with an approximate 20-25% or greater lifetime risk, including women with a strong family history of breast or ovarian cancer and women who received RT to the chest for Hodgkin’s Disease.
Risk Factors

- Age and onset of menstruation and menopause
- Gender
- Ethnicity
- Benign breast disease
- Personal history of breast cancer
- Lifestyle and dietary factors
- Reproductive and hormonal factors
- Family history and genetic factors
- Environmental factors
Age and Gender

- 100 x more frequent in women than men
- When breast cancer occurs in men it is often related to the BRCA 2 genetic mutation.
- In Women, the incidence rises sharply with age until age 50 where the curve becomes less steep. The curve flattens at ages 75-80, but risk continues to increase with age and screening should be lifelong.
Race and Ethnicity

- Breast cancer is the most common cancer across every major ethnic group. There are interracial differences.
- The highest rate occurs in white women, followed by blacks, Asian Americans, Hispanics, and American Indians.
- Socioeconomic factors are influential
- Genetic and biologic factors may also contribute
Racial differences

• Black women have a younger age peak than white women.
• Black women tend to have a more advanced stage at diagnosis and higher stage specific mortality.
• Some data suggests black women have more aggressive cancers (triple negative cancers).
Socioeconomic Class

• Surprisingly if higher socioeconomic class there is an increased risk thought to be related to delayed child-bearing, age at first birth, nulliparity.

• Decreased use of screening mammography in women of lower socioeconomic class often leading to diagnosis at a more advanced stage.
Pre-malignant Benign Breast Disease

- Multiple non-proliferative breast lesions
- Proliferative breast lesions with atypia
- Atypical Ductal Hyperplasia (ADH)
- Atypical Lobular Hyperplasia (ALH)
- Lobular Carcinoma In Situ (LCIS)
- Women with any of these histologic diagnoses should be referred to a medical oncologist to discuss chemoprevention.
Personal History of Breast Cancer

- The risk of developing breast cancer increases by
- 1% per year in premenopausal women
- 0.5% per year in postmenopausal women

- The risk does not increase indefinitely. Tops off around 20% in sporadic cases
BMI

• The higher the weight, the greater the risk of breast cancer in post menopausal women.
• Significant weight gain after menopause increases risk.
• This is due to higher circulating levels of estrogen as the more adipose tissue there is, the increased conversion of estrogen precursors to estrogen.
• Obese women also have a higher risk of dying of cancer
Reproductive and Hormonal Factors

- Younger age at menarche
- Later menopause
- Later first pregnancy
- Lower parity
- Bilateral oophorectomy by the age of 40 reduces a woman’s lifetime risk by 50%, but no benefit if HRT given
Family History of Breast Cancer

- Not synonymous with an inherited genetic mutation.
- Most families with a history of breast cancer do NOT have genetic mutations causing the disease. Risk in women without a genetic mutation is 1.5 – 3x if one 1st degree relative with breast cancer.
- Families with MULTIPLE members of breast or ovarian cancer at a young age are at greater risk of carrying a genetic mutation.
Probability of Inherited Susceptibility

• Family history – 20-30% have at least one relative with the disease
• 5-10% are BRCA +
  – These genes are inherited in an autosomal dominant fashion and function as tumor suppressor genes
  – Hereditary breast cancers arise from MUTATIONS in the BRCA 2 and BRCA 2 genes.
BR CA Breast Cancer Risk correlates with

- 1\textsuperscript{st} degree relatives most significant, then 2\textsuperscript{nd} and 3\textsuperscript{rd} degree
- Number of affected relatives
- Age at which the breast cancer occurred
- Bilaterality of the disease in affected relatives
- Family history of Ovarian Cancer
BRCA 1 and BRCA 2 Mutations

- BRCA mutations are found in between 1-3.3% of American women unselected for family history and accounts for 5-10% of all breast cancers.
- The impact of these mutations is far greater in selected patient populations.
  - Ex. Among Ashkenazi Jewish women 12-30% of breast cancers are thought to be BRCA 1 or BRCA 2 related.
Suspect Genetic Mutations:

- When multiple relatives have breast cancer, particularly when disease begins at young age, or family history of other cancers, especially ovarian.
- Germline mutation of a tumor-suppressor gene from either maternal or paternal side.
- Autosomal dominant inheritance
BRCA 1

- Located on chromosome 17
- 50% risk of breast cancer by age 45
- 85% lifetime risk of breast cancer
- Over 80 distinct mutations of BRCA 1 have been identified in high risk families.
BRCA 2

• Identified on Chromosome 13
• Associated with early onset breast cancer but not as early onset ovarian cancer
• Often seen in male patients with breast cancer
Ashkenazi Jewish Descent

- There are three specific mutations of BRCA 1 and BRCA 2 that are most often seen in Ashkenazi Jewish women.
- For most Jewish women, testing for these specific mutations is enough.
- Ashkenazi Jewish women have a 2% chance of carrying a BRCA 1 or BRCA 2 mutation.
Genetic Testing

• Genetic testing is the only way to identify the presence of BRCA mutations in a given patient.

• Hopefully with molecular profiling we may discover pathologic features to suggest or exclude their presence.
## Risk of breast cancer

<table>
<thead>
<tr>
<th></th>
<th>Percent of population</th>
<th>Percent of all breast cancer cases</th>
<th>Average lifetime risk of breast cancer, percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>~90</td>
<td>80 to 85</td>
<td>11 to 12</td>
</tr>
<tr>
<td>Positive family history breast cancer*</td>
<td>~12</td>
<td>15 to 20</td>
<td>20 to 25</td>
</tr>
<tr>
<td>Positive BRCA1 or 2 mutation</td>
<td>~0.1</td>
<td>5 to 6</td>
<td>65 to 85</td>
</tr>
</tbody>
</table>

* Breast cancer in a first-degree relative.
<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Estimated lifetime risk in BRCA1 mutation carriers</th>
<th>Estimated lifetime risk in BRCA2 mutation carriers</th>
<th>Lifetime risk in general population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer [2]</td>
<td>47 to 66 percent*</td>
<td>40 to 57 percent*</td>
<td>12.5 percent</td>
</tr>
<tr>
<td>Contralateral breast cancer [1]</td>
<td>Up to 65 percent</td>
<td>Up to 50 percent</td>
<td>0.5 to 1 percent per year</td>
</tr>
<tr>
<td>Ovarian cancer[2]</td>
<td>35 to 46 percent</td>
<td>13 to 23 percent</td>
<td>1.5 percent</td>
</tr>
<tr>
<td>Colon cancer [1]</td>
<td>Not increased, or increased very slightly</td>
<td>Not increased, or increased very slightly</td>
<td>5 percent</td>
</tr>
<tr>
<td>Prostate cancer[1]</td>
<td>Elevated (risk unknown)</td>
<td>35 to 40 percent</td>
<td>15 percent</td>
</tr>
<tr>
<td>Male breast cancer[3]</td>
<td>0.2 to 2.8 percent</td>
<td>3.2 to 12 percent</td>
<td>0.1 percent</td>
</tr>
<tr>
<td>Pancreatic cancer[1]</td>
<td>&lt;10 percent</td>
<td>&lt;10 percent</td>
<td>1.3 percent</td>
</tr>
</tbody>
</table>
Gail Model – Breast Cancer Risk Assessment Tool

- Age at Menarche
- Age at First Live Birth
- Number of previous breast biopsies
- Presence of Atypical hyperplasia in bx
- Number of First Degree Relatives with breast cancer
- Race
Gail Model

• Allows physicians to calculate whether the benefit of chemoprophylaxis with tamoxifen for five years outweighs the risks of the drug. (DVT, PE, slight increased risk of endometrial cancer).

• Tamoxifen is still the ONLY medication approved for the prevention of breast cancers.
Breast Cancer in the 21st Century

• We see significant improvements in local-regional control in these past ten years with reduced morbidity.

• We have improved systemic treatment for breast cancer and newer ways of giving the treatments. (i.e. taxanes, dose dense treatments and neo-adjuvant treatment.)

• Targeted therapies such as herceptin and aromatase inhibitor therapy for receptor positive disease have been developed.
Genomic Studies

• We are breaking the code of the tumor genome which has the potential to significantly change our understanding and treatments of breast cancer.

• Initial genomic studies identified basic subtypes of breast cancers, including the luminal, basal-like, and her-2-neu subtypes.
Molecular Profiling

• Doing genomic studies on each individual’s tumor will provide the physician with information on what drives each individual’s malignancy. This can lead to a more individualized therapy.

• Identification of the molecular profile of a particular tumor will allow therapy to be directed at these identified markers with improved efficacy and decreased toxicity.
With newer therapies...

- Patient safety is improved.
- There is reduced risk of recurrence.
- This relates to improved survival.
Signs and Symptoms of Breast Cancer

- Often none
- Palpable lump, may be painful, may be mobile or fixed to chest wall
- New nipple retraction or inversion
- Skin dimpling or redness
- Nipple discharge – bloody or not
- Mammographic changes
Clinical Breast Evaluation

- Breast mass – size, location, consistency, fixation to skin, muscle or chest wall.
- Skin changes – erythema, edema, dimpling, subq nodules, ulceration
- Nipple changes – retraction, discoloration, erosion, discharge (color?)
- Nodes – axillary – size, number, fixation; supraclavicular, infraclavicular
Breast Cancer Pathology

• These are the tests that have been used to characterize breast cancers. They remain important.
  – Tumor histology
  – Tumor grade
  – IHC analysis of hormone receptors
  – IHC analysis of human epidermal growth factor over expression. Verify with FISH.
Other Prognostic Indicators

- ER/PR Positivity
  - Good. Predicts responsive to hormonal Rx

- HER-2-Neu Overexpression
  - Historically “bad”, but predicts response to Herceptin which has changed the tumor’s behavior

- Proliferation rate/grade (Ki 67)
  - Lower is better

- Oncotype DX: Recurrence Score

- Mammaprint Score (High or Low Risk)

- Triple Negative is the Highest Risk Group
Breast Cancer Intrinsic Subtypes

- Luminal
  - Luminal A
  - Luminal B
- HER 2 Enriched
- Basal Like
Luminal Breast Cancers

- The most common of all subtypes, comprising approximately 2/3 of all breast cancer.
- **Luminal A** subtype is twice as common as luminal B subtype.
  - In luminal A tumors the ER expression is generally higher than in Luminal B tumors and the proliferation gene expressions are generally lower in luminal A than in luminal B (her-2-neu).
- **Luminal B** tumors tend to be more highly proliferative and have lower expression of ER and ER regulated genes.
Luminal A Tumors

• ~40% of all breast cancers
• High expression of ER related genes
• Low expression of Her 2 related genes
• Low expression of the proliferation genes (Ki 67)
• These carry the best prognosis of all breast cancer subtypes
Luminal B Tumors

- ~20% of all breast cancers
- Lower expression of ER related genes
- Variable Her 2 expression
- Higher expression of the proliferation genes
- Often have a high Recurrence Score
Her 2 Enriched

- 10-15% of breast cancers
- High expression of Her-2 and proliferation gene clusters. Low expression of the luminal clusters
- Generally receptor - and Her 2 +
- Natural history of this type of breast cancer has been altered by the targeted therapy herceptin
Basal-like

- 10-15% of all breast cancers
- Generally the “triple negative” breast cancers
- Similarity in expression as the basal epithelial cells
- High expression of proliferation gene clusters
- Associated with BRCA 1 mutation
- More common in premenopausal Black women
- ABSENCE of targeted therapy in this subtype is a real treatment obstacle
Case Study

• A 39 year old woman goes for her routine screening mammogram. It shows micro calcifications. Special views are requested and they reveal an irregular solid lesion, birads 5. Biopsy is recommended.
Biopsy Techniques

• FNA – Rapid, painless and cost-effective. Will not distinguish DCIS from Invasive Cancer nor is there histologic detail. Can have false negatives.

• Core Biopsy – Rapid, painless and cost-effective. False negatives and insufficient specimens does occur

• Excisional Biopsy – more painful and costly, avoids insufficient samples and false negatives. If clear margins, can be the “lumpectomy”.
Patient’s journey after a + biopsy

• Referral to a breast surgeon or to a general surgeon experienced in breast cancer surgery
• Refer for BRCA 1 and BRCA 2 testing. Why? Because it would be important to know her BRCA status before making the surgical decision.
• We check for the BRCA genes in most women who have breast cancer prior to the age of 45.
Surgical Procedures

• **Lumpectomy**
  – Removes only the tumor and an area surrounding the tumor.
  – Allows maintenance of normal cosmetic appearance
  – Requires post-op RT in most cases

• **Mastectomy**
  – Removes entire breast
  – Recommended for large or multi-focal tumors
  – For women who choose to avoid RT

• **Sentinel Lymph Node Biopsy**
  – Identifies lymph nodes most likely to be involved and if negative, patients can avoid an axillary dissection.
Surgical Treatment

- Breast conservative surgery has replaced the mastectomy as the most common procedure to treat the primary tumor.
- Nodal staging has changed with the lymphatic mapping for the sentinel node. This greatly reduces the morbidity of the axillary node dissection in sentinel node negative patients.
Staging

• Stage I – tumor 2 cm or less, no + nodes
• Stage II – >2cm AND <5cm tumor, neg nodes or smaller tumor with + nodes
• Stage III – Tumor > 5 cm or 4+ nodes or tumor involving chest wall or skin
• Stage IV – any distant metastasis
5 year survival by stage

- Stage I – 98%
- Stage II – 86%
- Stage III – 60%
- Stage IV 20%

- 62% Stages I and II at diagnosis
- 30% Stage III at diagnosis
- 6% Stage IV at diagnosis
- 2% Unstaged

Radiation Therapy

• Definitive RT is the standard for patients with early breast cancer in patients who elect breast conservative therapy. This significantly reduces the risk of local recurrence. This consequently reduces the risk of breast cancer mortality.

• We are now able to use partial breast irradiation in selected patients using brachytherapy.
Radiation Therapy

• High energy beam aimed at the target which causes molecular changes in cancer cells, resulting in cell death.

• Used in early stage breast cancer
  – After lumpectomy
  – After mastectomy for large tumors
  – Daily for 6 weeks
  – Mammosite (brachytherapy) treatment in 5 days
Radiation Therapy

• Used in metastatic breast cancer
  – To palliate painful bony metastasis and prevent pathologic fractures
  – Control of brain metastasis
Breast Cancer is Systemic at Presentation

- Microscopic Metastatic Disease is what is responsible for ultimate relapse of breast cancer.
- Tumors are heterogeneous.
- Some cell populations are resistant to certain chemotherapy agents while others are sensitive.
Systemic Therapy

• Adjuvant hormonal Therapy
  – Tamoxifen in premenopausal
  – Aromatase Inhibitor (Arimidex or Femara) in postmenopausal women ONLY

• Adjuvant chemotherapy
  – Of greater benefit in receptor negative breast cancer
  – Of limited benefit at times and genomics is helping determine the patients in whom systemic adjuvant chemotherapy would benefit.
Breast Cancer Biology

- Breast cancer is a heterogeneous disease. Hormone receptors are important. Other markers such as her-2-neu are also predictive of tumor biology which has been altered by therapy directed at this “target”. We have discovered that gene expression profiling increases our understanding on risk, prevention and treatment.
The role of the Oncotype DX® assay in breast cancer management
Case study presentation

• A 55-year-old post-menopausal woman presents with an infiltrating ductal carcinoma
  – Tumor size 1.0 cm
  – ER/PR IHC positive
  – HER2 IHC negative
  – Sentinel lymph node negative
  – Excellent overall health

How should this patient be evaluated for treatment?
What is her risk of disease recurrence?
How likely is she to benefit from hormonal or chemotherapy?
Breast cancer treatment in the United States (2009)

• Approximately 110,000 women with ER+, lymph node-negative breast cancer are diagnosed annually in the United States
  – This represents ~50% of newly diagnosed patients today
  – Many women are offered chemotherapy, but all do not receive substantial benefit

Better identification of disease markers is needed to help make therapeutic decisions
Prognostic & predictive markers utilized in breast cancer management

**Prognostic (recurrence risk)**
- Axillary node status
- Histologic type/grade
- Tumor size
- Patient age
- Lymphatic/Vascular invasion
- ER/PR status
- HER2 neu status
- Oncotype DX® test

**Predictive (treatment benefit)**
- ER/PR status
- HER2 neu status
- Oncotype DX® test

*These markers can be used to estimate the risk of disease recurrence*

*These markers can be used to predict treatment benefit*

Oncotype DX® Report Samples

- Oncotype DX report provides valuable information on:
  - Clinical prognosis
  - Predicted chemotherapy benefit
  - Quantitative data on ER / PR / HER2

- Node positive report contains an additional page with prognosis and predicted chemo benefit information specific to node-positive patients
Oncotype DX® gene panel was developed from clinical trial evidence

- 250 cancer-related genes were selected
- Genes were analyzed for expression and relapse-free interval correlations across 3 independent studies of 447 breast cancer patients

From these studies, 21 genes were selected

OncoType DX® Recurrence Score® result: calculated from 21 different genes

16 CANCER RELATED GENES

Estrogen
ER
PR
Bcl2
SCUBE2

Proliferation
Ki-67
STK15
Survivin
Cyclin B1
MYBL2

HER2
GRB7
HER2

Invasion
Stromelysin 3
Cathepsin L2

Others
CD68
GSTM1
BAG1

5 REFERENCE GENES

Beta-actin
GAPDH
RPLPO
GUS
TFRC
The Oncotype DX® Recurrence Score® result is a continuous predictor of recurrence risk.

What is the 10-year probability of distant recurrence for a patient with a Recurrence Score of 30?

Recurrence Score 30 = 20% risk of distant recurrence at 10 years.
Oncotype DX® Recurrence Score® result calculation and risk categories

**Recurrence Score** =

\[ \text{Recurrence Score} = + 0.47 \times \text{HER2 Group Score} \]
\[ - 0.34 \times \text{Estrogen Group Score} \]
\[ + 1.04 \times \text{Proliferation Group Score} \]
\[ + 0.10 \times \text{Invasion Group Score} \]
\[ + 0.05 \times \text{CD68} \]
\[ - 0.08 \times \text{GSTM1} \]
\[ - 0.07 \times \text{BAG1} \]

**Risk group**

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Recurrence Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>&lt; 18</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>18 - 30</td>
</tr>
<tr>
<td>High risk</td>
<td>≥ 31</td>
</tr>
</tbody>
</table>

Clinical validation of Oncotype DX® breast cancer assay in node-negative disease
Oncotype DX® clinical validation: conclusions, NSABP B-14

- Oncotype DX® Recurrence Score® result is validated as a predictor of recurrence in node-negative, ER+ patients.
- Oncotype DX Recurrence Score performance exceeds standard measures (patient age, tumor size, and tumor grade).
- Oncotype DX Recurrence Score result (based on tumor gene expression) more accurately quantifies the risk of distant recurrence than do the NCCN guidelines (based on patient age, tumor size, and tumor grade).

High Recurrence Score® result correlates with greater benefit from chemotherapy (NSABP B-20)

RS, Recurrence Score result

<table>
<thead>
<tr>
<th>Group</th>
<th>Tamoxifen + chemotherapy</th>
<th>N</th>
<th>Events</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td></td>
<td>424</td>
<td>33</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Tamoxifen</td>
<td>227</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>RS &lt; 18</td>
<td></td>
<td>218</td>
<td>8</td>
<td>0.61</td>
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<tr>
<td></td>
<td>Tamoxifen + chemotherapy</td>
<td>135</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tamoxifen</td>
<td>117</td>
<td>13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RS 18-30</td>
<td></td>
<td>89</td>
<td>9</td>
<td>0.39</td>
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<td></td>
<td>Tamoxifen + chemotherapy</td>
<td>45</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Tamoxifen</td>
<td>47</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

PATIENTS WITH HIGH RS
28% absolute benefit from tamoxifen + chemotherapy

4.4% absolute benefit from tamoxifen + chemotherapy
ASCO guidelines on the use of tumor markers in breast cancer

- Oncotype DX® testing can be used to determine prognosis in newly diagnosed patients with node-negative, estrogen receptor-positive breast cancer who will receive tamoxifen.

1. To predict risk of recurrence in patients considering treatment with tamoxifen.
2. To identify patients who are predicted to obtain the most therapeutic benefit from adjuvant tamoxifen and may not require adjuvant chemotherapy.
3. Patients with high Recurrence Score® result appear to achieve relatively more benefit from adjuvant chemotherapy (specifically CMF) than tamoxifen.

- Conclusions may not be generalizable to hormonal therapies other than tamoxifen or to other chemotherapy regimens.

Recurrence Score® result is prognostic for node-positive patients (tamoxifen arm)

**DFS by risk group (tamoxifen-alone arm)**

- RS < 18 (n = 55)
- RS 18-30 (n = 46)
- RS ≥ 31 (n = 47)

**OS by risk group (tamoxifen-alone arm)**

- RS < 18 (n = 55)
- RS 18-30 (n = 46)
- RS ≥ 31 (n = 47)

**Stratified log-rank P = 0.017 at 10 years**

**Stratified log-rank P = 0.003 at 10 years**

**10-Year DFS**: 60%, 49%, 43%

**10-Year OS**: 77%, 68%, 51%

RS, Recurrence Score result
68-year-old patient with 1.1-cm tumor

- **Menopausal Status**: Postmenopausal
- **Tumor Type**: Infiltrating Ductal Carcinoma (IDC)
- **Tumor Size**: 1.1 cm
- **ER Status (IHC)**: Positive
- **PR Status (IHC)**: Positive
- **HER2/neu Status**: Negative
- **Histologic Grade**: 2
- **Lymph Node Status**: Negative
- **General Health**: Fair
RESULTS

Recurrence Score = 34

CLINICAL EXPERIENCE

Patients with a Recurrence Score of 34 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 23% (95% CI: 18%-28%).
69-year-old patient with 1.3-cm tumor

- **Menopausal Status:** Postmenopausal
- **Tumor Type:** Infiltrating Ductal Carcinoma (IDC)
- **Tumor Size:** 1.3 cm
- **ER Status (IHC):** Positive (2)
- **PR Status (IHC):** Positive (2)
- **HER2/neu Status:** Negative (IHC)
- **Histologic Grade:** 3
- **Lymph Node Status:** Negative
- **General Health:** PS 0
RESULTS

Recurrence Score = 11

CLINICAL EXPERIENCE

Patients with a Recurrence Score of 11 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 7% (95% CI: 5%-10%).
54-year-old patient with 1.7-cm tumor

- **Menopausal Status**: Postmenopausal
- **Tumor Type**: Infiltrating Ductal Carcinoma (IDC) With Ductal Carcinoma In Situ (DCIS)
- **Tumor Size**: 1.7 cm
- **ER Status (IHC)**: Positive
- **PR Status (IHC)**: Positive
- **HER2/neu Status**: Negative (3+ by IHC)
- **Histologic Grade**: 2
- **Lymph Node Status**: Negative (0/4)
- **General Health**: Very good
RESULTS
Recurrence Score = 72

CLINICAL EXPERIENCE
Patients with a Recurrence Score of 72 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 36% (95% CI: 25%-46%).

*For Recurrence Scores > 50, group average rate of distant recurrence and 95% CI shown.
Gene-Expression Signature Predicts Survival in Breast Cancer

- 70 gene prognosis profile
- Patients classified as having either a poor prognosis or good prognosis signature.
- The gene expression profile studied is a more powerful predictor of the outcome of disease in young patients with breast cancer than standard systems based on clinical and histologic criteria.
Mammaprint 70 gene profile

- Performed best as a predictor of the appearance of distant metastases during the first five years after treatment.
- It appears by the mammaprint data that the ability to metastasize to distant sites is an early and inherent genetic property of breast cancer.
- Data suggest that classification of patients into low and high risk can help guide therapeutic decisions.
The 21\textsuperscript{st} Century is an exciting time in oncology!
Thank you