The Changing Landscape of Breast Cancer Management and Treatment

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Objectives

• Review current screening recommendations
• New surgical approaches
• Genetics
  – Familial
  – Tumor
• Treatment approaches
Breast Cancer Mortality Statistics

• Over 220,000 women diagnosed in the US annually

• About 42,000 die of breast cancer- second most common cause of death from cancer in women

• Between 1990 -2007 mortality decreased 36%
  – Combination of screening and improved treatment
How Many People Survive 5 Years Or More after Being Diagnosed with Female Breast Cancer?

Surviving 5 years - **89.7%**

All stages combined
Survival by Stage

Regional includes positive lymph nodes - Stage 2B and 3
14% decrease in 5 years survival
50 is an *Artificial* line

- The incidence of breast cancer gradually increases with every year in age
- There is no sharp increase at 50
- Women 45-55 have a very similar incidence of breast cancer hence the American Cancer Society recommendations for discussion at 40 but definitely start yearly screening at 45
Biggest Myth In Assessing Breast Cancer Risk

Myth- High risk only if family history of breast cancer

Fact- 80% of women who develop breast cancer have no family history
Environment and Lifestyle risk

- Obesity
- Exercise
- Alcohol intake
- Fruits and Veggies
- Age at first child or no children
- Tobacco
Screening Recommendations

• Remember 40 to consider starting screening
  – Definitely at 45
• Every year 45-55 versus every other year > 55
• Self exam
• Dense Breast
  – Add additional imaging
• Family history is not the whole story
Oregon’s Breast Density Law (SB 420)

• Effective January 2014
• Imaging centers must provide information
  – inform patient of breast density based on BIRADS
  – Alert patient that density can increase cancer risk
  – That density may obscure cancer on mammogram
  – Inform patient that other modalities may improve screening in dense breast

• Discuss your density with your doctor to see if additional modalities are indicated
Look up her mammogram report (different from the patient letter).

1. If the report states her density is *heterogeneously dense*, this is associated with minimal risk above average (RR=1.2 compared to average breast density).

2. If her density is *extremely dense*, this factor doubles her risk of breast cancer compared to average density, similar to the risk associated with a family history of unilateral, post-menopausal breast cancer in a mother, sister, or daughter. For example, having *extremely dense* tissue on its own raises the 10-year risk of breast cancer in the average 50 year old woman from 1 in 42 to 1 in 21.
Addressing Breast Density

- Discuss with your provider
  - Ultrasound
    - Automated Breast Ultrasound or ABUS
  - Breast MRI
    - Skilled Breast Imager
  - Molecular Breast Imaging
    - BSGI
Familial Genetic Risk

• Only about 10-15% of breast cancer is currently thought to be genetic or inherited from family.

• Learning that many other familial cancers can relate back to breast cancer.
Partial List of Mutations associated with Breast Cancer

- BRCA 1 & 2
- P53- Li- Fraumeni
- PTEN –Cowden’2
- CHEK2
- PALB2
- ATM
- NBS1
- RAD50
- BRIP
- CDH1
What is panel testing?
Tumor Genetics

• Cancers have genetic mutations
  – Occur as result of environmental exposure

• Genetic mutations in cancer can give us targets for therapy

• In breast cancer give info on type of treatment needed
Prognostic factors

• Estrogen Receptor
• Progesterone receptor
• Her2neu
  – IHC
  – FISH
• Ki-67(MIB)
• p53

• Best Prognosis are Strongly ER+/PR+ tumors
• Worst Prognosis is Triple Negative
• Her2neu is aggressive but currently good targeted therapies
Traditional Ideas meet Genomics and Proteomics

**Old paradigm**

• Halsted and tumor extirpation
  – Cancer can be controlled by aggressive local therapy
  – Stage and number of nodes is paramount to predicting prognosis

**New paradigm**

• Breast cancer is a systemic disease
  – Systemic therapy controls cancer
    • Neoadjuvant benefits
  – Molecular markers can predict prognosis and best treatment
    – *Response to therapy predicts outcome*
OncotypeDX - 21 (16) Gene Assay
Interrogation of critical genomic pathways

1. Growth and proliferation
3. Local invasion
7. Adaptation to microenvironment at secondary site
B-20: Absolute % Increase in DRFS at 10 Years

- Benefit of Chemo Depends on RS

<table>
<thead>
<tr>
<th>RS</th>
<th>Number</th>
<th>% Increase in DRFS at 10 Yrs (mean ± SE)</th>
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<tbody>
<tr>
<td>RS&lt;18</td>
<td>353</td>
<td>0% ± 10%</td>
</tr>
<tr>
<td>RS18-30</td>
<td>134</td>
<td>10% ± 20%</td>
</tr>
<tr>
<td>RS≥31</td>
<td>164</td>
<td>20% ± 30%</td>
</tr>
</tbody>
</table>

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MammaPrint - 70 Gene Assay
Interrogation of critical genomic pathways

1. IGFBP5, TGFβ3, FGF18, ESM1, RARRES3, PITRM1, EXT1, EXT3, SCUBE2, EBF4, CDC42BPA, CDC47L, GMPS, MELK, RFC4, WISP1, HRASLS, BBC3, DTL, FBXO31, EGLN1, GNAZ, MTDH, FLT1, ECT2, DIAPH3, NUSAP1, AKAP2, NDC80, PRC1, ORC6L, CENPA, DCK, CCNE2, MCM6, QSOX2, STK32B

2. COL4A2, FLT1, FGF18, MMP9

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Interrogation of critical genomic pathways
Treatment Before Surgery

- Measure response to treatment
- Response to treatment is the largest predictor of outcome
- Large paradigm change
- Both chemo and endocrine therapy can be given first
Residual Cancer Burden

ER-Negative

ER-Positive

Proportion Free of Distant Relapse

Time (months)

0.001

0.2

0.4

0.6

0.8

1.0

P < 0.001

0

20

40

60

80

Time (months)
Changes in Surgical Management
Surgical Options

- Cryo ablation- Not ready for prime time
- Lumpectomy or breast conservation
  - Oncoplastic approach
- Mastectomy
  - Nipple sparing or not
  - Reconstruction or not
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Oncoplastics

• More than removing the tumor
• Think of long term result
• Large breasts
• Small breasts- large area for removal or location
• Pendulous breasts
Managing Large Pendulous Breast

• Partial mastectomy and bilateral reduction mammoplasty.
  – Facilitates radiation therapy.
  – Less fibrosis.
  – Symmetry preserved.
Macromastia
Focus of Quality of Life Post Treatment

- Improved aesthetic outcomes after mastectomy or breast conservation
- Lower risk of lymphedema
- Reduce symptoms of treatment from chemo and endocrine therapy
Axillary Reverse Mapping

- Theory into practice
  - Identify lymphatics draining the arm
  - Avoid injury to arm lymphatics
  - Little cross over between arm and breast lymphatics
  - Maintaining lymphatics will reduce clinical lymphedema
Prospective trials on ARM

- 265 patients
  - 127 - traditional ALND
  - 138 - ARM with ALND
- ARM performed with radioactive tracer and methylene blue
- ARM nodes evaluated with FNA in OR

Results
- ARM successful in 129 cases (93%)
- ARM nodes positive in 11 (8%)

Number of nodes removed
- Control- 20.7
- ARM -20.3

Lymphedema at 2 years
- Control- 42 patients or 33% incidence
- ARM- 7 patients or 5%

Tao Yue et al: Clinical Breast Cancer, Vol. 15, No. 4, 301-6
National Moonshot

• Future progress
  – Prevention
  – Less intervention
  – Improved screening options including blood or breath analyzer
  – Genetics
  – Personalized care and tumor targeting