Contemporary Management of Breast Cancer

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Jessica Maxwell, MD, MSc, FRCSC; Brenda C. Ram, CMP, CHCP Sara M. Weber, MSW, CHES®, CBE Jackie Siebels, BSN, RN-BC
Disclosures

• No real disclosures other than…
  
  • Management of breast cancer is *complex*
  
  • Research is rapidly informing and changing the way we practice
  
  • Guidelines are changing quickly
Series of Activities Available Online

UNMC-CCE offers topics of interest to medical professionals that are available online for CME credit at:

www.unmc.edu/cce/outreach

If you have questions, please contact Sara Weber.
Objectives

1. Identify breast screening criteria for average and high risk patients.


3. Understand the rationale for surgical consultation in high risk benign lesions.

4. Review surgical options for treatment and their applicability to specific patients.

5. Recognize the importance of multidisciplinary care and, surveillance, and survivorship issues in this setting.
Breast Screening

• Mammogram = screening test of choice for breast cancer

• Different guidelines make different recommendations

• Consider your patient’s individual risk factors, insurance coverage

• Vast majority of our patients undergo annual screening starting at 40 years old
# Average Risk Screening

<table>
<thead>
<tr>
<th></th>
<th>USPSTF&lt;sup&gt;1&lt;/sup&gt; 2009</th>
<th>ACS&lt;sup&gt;2&lt;/sup&gt; 2015</th>
<th>NCCN&lt;sup&gt;3&lt;/sup&gt; 2017</th>
<th>ASBS&lt;sup&gt;4&lt;/sup&gt; 2015</th>
<th>ACR&lt;sup&gt;5&lt;/sup&gt; 2016</th>
<th>ACOG&lt;sup&gt;6&lt;/sup&gt; 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Begin</strong></td>
<td>50</td>
<td>45 with opportunity to begin at 40</td>
<td>40</td>
<td>45 with opportunity to begin at 40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>Biennial</td>
<td>Annual to 54, then biennial with opportunity to continue annually</td>
<td>Annual</td>
<td>Annual to 54, then biennial</td>
<td>Annual</td>
<td>Annual or Biennial – SDM*</td>
</tr>
<tr>
<td><strong>End</strong></td>
<td>75</td>
<td>Biennial after 75 if life expectancy &gt;10 years</td>
<td>Individual</td>
<td>Biennial &gt;75 if life expectancy &gt;10 years</td>
<td>Individual</td>
<td>Individual – SDM*</td>
</tr>
</tbody>
</table>

*SDM = shared decision making
<table>
<thead>
<tr>
<th>Reproductive Factors</th>
<th>Hormonal Factors</th>
<th>Lifestyle Factors</th>
<th>Other Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early menarche</td>
<td>OCP use</td>
<td>Increased BMI</td>
<td>Family history</td>
</tr>
<tr>
<td>Late age at first birth</td>
<td>HRT use</td>
<td>Alcohol use</td>
<td>Ashkenazi Jewish heritage</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>Sedentary lifestyle</td>
<td></td>
<td>Previous thoracic radiation &lt;30yo</td>
</tr>
<tr>
<td>Late menopause</td>
<td>High saturated fat intake</td>
<td>Previous ADH, ALH, LCIS or FEA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low fruit and vegetable intake</td>
<td>Mammographic breast density</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Genetic mutations</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Previous breast biopsy</td>
<td></td>
</tr>
</tbody>
</table>
Risk Assessment Models

• Gail Model
  • Estimates 5 year risk of invasive breast cancer and lifetime risk
  • Uses personal, reproductive and family history
    • First degree relatives only
  • Women >35yo
  • Without history of:
    • DCIS or LCIS
    • Previous radiation
  • Validated in Caucasian women
    • May underestimate risk in African American or Hispanic women
  • Available online:
    • NCI Breast Cancer Risk Assessment Tool
      • Based on the Gail Model
# NCI Breast Cancer Risk Assessment Tool

(Click a question number for a brief explanation, or read all explanations.)

1. Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) or has she received previous radiation therapy to the chest for treatment of Hodgkin lymphoma?

2. Does the woman have a mutation in either the *BRCA1* or *BRCA2* gene, or a diagnosis of a genetic syndrome that may be associated with elevated risk of breast cancer?

3. What is the woman's age?  
   This tool only calculates risk for women 35 years of age or older.

4. What was the woman's age at the time of her first menstrual period?

5. What was the woman's age at the time of her first live birth of a child?

6. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?

7. Has the woman ever had a breast biopsy?
   
   7a. How many breast biopsies (positive or negative) has the woman had?

   7b. Has the woman had at least one breast biopsy with atypical hyperplasia?

8. What is the woman's race/ethnicity?

8a. What is the sub race/ethnicity?

---

Calculate Risk »
Risk Assessment Models

• Tyrer-Cuzick Model
  • More comprehensive
  • Uses personal, reproductive and more extensive family history
  • Also includes:
    • Mammographic density
    • BRCA mutation
    • Previous benign biopsy
      • Hyperplasia
      • Atypia
      • LCIS
Tyrer-Cuzick Model

Personal factors:
- Woman's age:
- Menarche:
- Height:
- Weight:
- Measurements:
  - Metric:
  - Imperial:
- Nulligravid:
- Parous:
- Unknown:
- Age:
- First child:
- Ovarian cancer:

Mammographic density (age 40+):
- % Yldpar® Volumetric Density
- % VAS Percentage Density
- BI-RADS® ATLAS Density

Ashkenazi Inheritance:
- Genetic Testing:
- Male relatives:
- Half sisters:
- Affected cousins:
- Affected nieces:
- Family history:

IBIS Risk Evaluator v8.0
Risk Assessment Models

- BOADICEA
  - Estimates probability of carrying of BRCA 1 or 2 mutations

- BRCAPRO
  - Estimates probability of carrying BRCA 1 or 2 mutations
High Risk Screening

Women who have a lifetime risk >20% as defined by models that are largely dependent on family history:

- Clinical encounter every 6-12 mo
  - to begin when identified as being at increased risk
  - Referral to genetic counseling if not already done
- Annual screening mammogram
  - to begin 10 years prior to the youngest family member but not less than age 30 y
  - Consider tomosynthesis
- Recommend annual breast MRI
  - to begin 10 years prior to youngest family member but not less than age 25 y
- Consider risk reduction strategies (See NCCN Guidelines for Breast Cancer Risk Reduction)
- Breast awareness

OR

Patient who receives thoracic RT between the ages of 10 and 30 y:

- Current age <25 y
  - Annual clinical encounter
    - beginning 8-10 y after RT
    - Breast awareness
  - Clinical encounter every 6-12 mo
    - Begin 8-10 y after RT
    - Annual screening mammogram
      - Begin 8-10 y after RT but not prior to age 25 y
      - Consider tomosynthesis
    - Recommend annual breast MRI
      - Begin 8-10 y after RT but not prior to age 25 y
    - Breast awareness

- Current age ≥25 y
  - Annual clinical encounter
  - Breast awareness
High Risk Screening

**SCREENING OR SYMPTOM CATEGORY**  
**Increased Risk:**

Women ≥35 y with 5-year Gail Model risk of invasive breast cancer ≥1.7%

- Clinical encounter\(^3,\!^\text{g}\), every 6–12 mo
  - to begin when identified as being at increased risk by Gail Model
- Annual screening\(^3\) mammogram\(^k\)
  - to begin when identified as being at increased risk by Gail Model
  - Consider tomosynthesis\(^3\)
- Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))
- Breast awareness\(^l\)

**OR**

Women who have a lifetime risk ≥20% based on history of LCIS or ADH/ALH

- Clinical encounter\(^3,\!^\text{g}\), every 6–12 mo
  - to begin at diagnosis of LCIS or ADH/ALH
- Annual screening\(^3\) mammogram\(^k\)
  - to begin at diagnosis of LCIS or ADH/ALH but not less than age 30 y
  - Consider tomosynthesis\(^3\)
- Consider annual MRI
  - to begin at diagnosis of LCIS or ADH/ALH but not less than age 25 y (based on emerging evidence)
- Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))
- Breast awareness
Why the Changes in Staging?

• Multidisciplinary panel of experts assessed published data and large unpublished databases

• Need to incorporate biologic factors into the staging system
  • Tumor grade
  • Proliferation rate (Ki67 index)
  • Receptor status (ER, PR, HER2)
  • Gene expression panels (Oncotype DX)

• Updates are to provide increased precision and flexibility of staging system and prognostic classification
When are the changes happening?

**NOW!**

- AJCC released the new staging system in March 2017
- Planned for full implementation of the system in January 2018
- All cases up to December 31, 2017 staged with 7th edition
- All cases after January 1, 2018 staged with 8th edition
What Are the Changes?
A Basic Overview:

- Tumor markers are now incorporated into the staging system
  - Refines prognosis
  - Practical treatment importance

- Genomic assays incorporated as well
  - Oncotype DX
  - May downstage some ER+ and node negative tumors

- Lobular carcinoma in situ (LCIS) has been removed
  - No longer considered Tis
  - Marker of increased risk, NOT a malignancy itself
What Stays the Same?

• Anatomic TNM staging remains a key element of the 8th edition
  • Based solely on the anatomic extent of disease
  • Recognized worldwide
  • Common language for tumor staging
  • Accessible worldwide
    • Much of the world does not have reliable access to biomarker assessment
Benign Lesions and Breast Cancer Risk

<table>
<thead>
<tr>
<th>NONPROLIFERATIVE: NO INCREASE IN RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cysts: micro or macro</td>
</tr>
<tr>
<td>Ductal ectasia</td>
</tr>
<tr>
<td>Simple fibroadenoma</td>
</tr>
<tr>
<td>Mastitis</td>
</tr>
<tr>
<td>Fibrosis</td>
</tr>
<tr>
<td>Metaplasia: squamous or apocrine</td>
</tr>
<tr>
<td>Mild hyperplasia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PROLIFERATIVE: RR 1.5–2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex fibroadenoma</td>
</tr>
<tr>
<td>Papilloma</td>
</tr>
<tr>
<td>Sclerosing adenosis</td>
</tr>
<tr>
<td>Hyperplasia: moderate or severe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PROLIFERATIVE WITH ATYPIA: RR 4.5–5.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical ductal hyperplasia</td>
</tr>
<tr>
<td>Atypical lobular hyperplasia</td>
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</tbody>
</table>

RR, relative risk.
### TABLE 74.3 INDICATIONS/CONTRAINDICATIONS

**INDICATIONS FOR SURGICAL BIOPSY AFTER CORE BIOPSY**

- Atypical ductal hyperplasia
- Atypical lobular hyperplasia
- Radial scar
- Lobular carcinoma in situ
- Columnar cell hyperplasia with atypia
- Papillary lesions
- Lack of concordance between appearance of mammographic lesion and histologic diagnosis
- Nondiagnostic specimen (including absence of calcifications on specimen radiograph when biopsy is performed for calcifications)
Great Resource!

Consensus Guideline on Concordance Assessment of Image-Guided Breast Biopsies and Management of Borderline or High-Risk Lesions
Surgical Options - Breast

Mastectomy

VS.

Lumpectomy or Partial Mastectomy
Mastectomy Options

- Simple mastectomy
- Skin sparing mastectomy with reconstruction
- Nipple sparing mastectomy with reconstruction
Who Needs a Mastectomy?

• Carriers of high risk genetic mutations
  • Only about 5% of the population

• High risk family history in the absence of genetic mutations

• Very young patients in the absence of genetic mutations
Who Needs a Mastectomy?

- Inflammatory cancer
- Large tumors or advanced disease
- Unfavorable tumor to breast ratio
  - i.e. large tumor in a small breast
- Previous radiation to breast/chest wall
Breast Conserving Therapy (BCT)

- BCT = lumpectomy + radiation
- Cornerstone in the management of breast cancer
  - Primary goal is complete excision of lesion to clear margins
  - Secondary goal is acceptable cosmesis
Why BCT?

• Survival outcomes are the same as mastectomy
• Local recurrence outcomes are similar to mastectomy
• Smaller surgery
  • Easier recovery
  • Fewer complications
• Preserve the breast
  • Less psychological stress and adjustment
• Mastectomy is *NOT MEDICALLY NECESSARY* in many patients
What is Oncoplastic Surgery (OPS)?

- **Oncoplastic breast surgery** = marriage of lumpectomy and local tissue rearrangement
  - Use patient’s own breast tissue to achieve a better aesthetic result

- **Goal** = complete resection of the lesion and excellent cosmesis in a single definitive procedure
What ISN’T Oncoplastic Surgery?

• Cosmetic surgery

• Tissue expander or implant based surgery

• Flap based reconstruction
  • Pedicle or free flap
  • Abdominal tissue most common
    • Latissimus as a salvage flap
How is OPS Different?

• Patient’s own breast tissue is stitched together to close the empty space left once the tumor is removed

• No empty space = no contour deformity

• Scar placement is more carefully chosen
  • Not just directly over the tumor

• Skin and breast tissue can be removed to provide a breast reduction or lift at the same time

• The opposite breast can be reduced or lifted to provide better symmetry
Why is it Important?

- 40% is a lot of women!\textsuperscript{8}

- Improved cosmesis leads to improved quality of life and psychologic and social functioning\textsuperscript{9,10}
  - Better body image
  - Improved sexuality and sexual function

- Patients generally do well and therefore have to live with the results of their surgery long term

- Focus on survivorship in breast cancer care
Contralateral Prophylactic Mastectomy

- **CPM** = removal of the unaffected (non-cancer) breast

- Rates are on the rise

- Only ~5% of the population carry a high risk genetic mutation

- Many CPMs are medically unnecessary
CPM Rates

Figure 1. Annual Nationwide Proportions of Contralateral Prophylactic Mastectomies (CPMs)

Annual nationwide percentages of CPMs among women with invasive unilateral early-stage breast cancer treated with surgery by age category, 2004-2012. The bars represent the percentage of CPMs among women treated with surgery for unilateral early-stage breast cancer. The vertical error bars represent 95% CIs.
CPM Rates

• The Midwest has the highest rates of CPM in the country\textsuperscript{11}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
State             & Overall (2004-2012), Patients, No. (%) & Year of Diagnosis, Patients, No. (%) & & & & \\
                  & Total Cases & CPM & 2004-2006 & Total Cases & CPM & 2010-2012 & Change Between Time Periods, PR (95% CI) \\
\hline
South Dakota      & 417 & 165 (39.6) & & 137 & 41 (29.9) & & 136 & 66 (48.5) & 1.62 (1.19-2.21) \\
Iowa              & 1644 & 532 (32.4) & & 614 & 132 (21.5) & & 474 & 213 (44.9) & 2.09 (1.74-2.51) \\
Colorado          & 2737 & 923 (33.7) & & 888 & 190 (21.4) & & 913 & 407 (44.6) & 2.08 (1.80-2.41) \\
Missouri          & 3341 & 868 (26.0) & & 1216 & 150 (12.3) & & 1028 & 443 (43.1) & 3.49 (2.96-4.12) \\
Nebraska          & 943 & 328 (34.8) & & 342 & 77 (22.5) & & 269 & 115 (42.8) & 1.90 (1.49-2.41) \\
\hline
\end{tabular}
\end{table}

• 42.8\% of women aged 20-44 with early stage, unilateral breast cancer underwent CPM between 2010 – 2012 in Nebraska\textsuperscript{11}
Surgical Options – Axilla

Sentinel Node Biopsy vs. Targeted Axillary Dissection vs. Complete Axillary Dissection
Sentinel Node Biopsy

• Safe and effective in surgical evaluation of the axilla\textsuperscript{12-14}
• Clinically node negative patients
• Allows for omission of axillary lymph node dissection (ALND) in some patients
  • Decreased risk of lymphedema compared to ALND
  • Lower risk of intraoperative complications
ACOSOG Z0011 Trial

• Practice changing
• Axillary dissection can safely be avoided in some node positive patients with no difference in DFS or LRR
  • 10 year follow up demonstrates overall survival in patients undergoing sentinel node biopsy alone is **NOT INFERIOR** to axillary node dissection
• Criteria:
  • cT1-2 N0 M0 disease
  • Breast conserving surgery
  • Adjuvant whole breast radiation
  • 1-2 sentinel nodes positive
Sentinel Node after Neoadjuvant Chemotherapy

- Accuracy of sentinel node biopsy after NAC has been investigated
  - ACOSOG Z1071\textsuperscript{17}, SENTINA\textsuperscript{18}, SN-FNAC\textsuperscript{19}
  - With dual tracer and removal of >2 LN, FNR is improved to <10%

- Was initially applied to patients who were node negative pre-chemotherapy

Table courtesy of Amanda Roberts, MD, MPH
Targeted Axillary Dissection

- Biopsy proven node positive patients
- Node clipped at biopsy
- Undergo neoadjuvant chemotherapy
  - Clinically node negative post chemo
- Clipped node localized (seed or wire) and removed
- Sentinel node biopsy performed
- Criteria:
  - Must localize clipped node
  - Must obtain at least 3 lymph nodes
  - Frozen section of all lymph nodes
Targeted Axillary Dissection

- Current protocol:
  - Any residual nodal disease on frozen section mandates completion ALND

- Technical feasibility has been demonstrated\textsuperscript{20}
- No long term data
- Has been widely adopted into practice
- In practice at our institution
Complete Axillary Node Dissection

• Still mandated in some patients
  • Residual nodal disease post systemic therapy
  • Inflammatory breast cancer
  • Significant burden of nodal disease on presentation
  • Occult breast cancer$^{21}$

• Alliance A011202 currently open and accruing
  • Phase III trial comparing axillary node dissection with radiation to axillary radiation alone in breast cancer patients with residual nodal disease post NAC
    • cT1-3 cN1 disease included
Post Treatment Surveillance

- **Clinical:**
  - History and physical 1 – 4x/year for 5 years
    - Then annually
  - Periodic screen for changes in family history
    - Genetics referral PRN
  - Educate and monitor for lymphedema
  - On Tamoxifen with uterus present: annual gynecologic evaluation
  - On aromatase inhibitor: bone mineral density at baseline and periodically

- **Imaging:**
  - Annual mammogram
    - Begin 6-12 months after completion of radiation
  - No role for routine imaging of reconstructed breasts
  - No role for routine imaging or labs for metastatic screening
Survivorship Issues

**Physical**
- Sexual Health (vaginal dryness, decreased libido)
  - 21% to >50% of patients
- Cognitive changes
  - During treatment >50%
  - After treatment 21-49%
- Premature menopause/hot flashes
  - >50%
- Chronic pain
  - 21 to >50%
- Arthralgias
  - 21-49%
- Osteopenia/Osteoporosis
  - >50%
- Peripheral neuropathy
  - 21-49%
- Lymphedema
  - 21-49%
- Fatigue
  - >50%

**Cognitive/Emotional**
- Distress, depression, anxiety, fear of recurrence
  - <20% to 49%
- Body image concerns
  - 21 to >50%
Nebraska Medicine Cancer Survivorship Clinic

• Referrals: 402-559-5600

• Locations:
  • Buffett Cancer Center
  • Village Pointe
  • Bellevue Medical Center

• Any patient who has completed active treatment for any cancer type

• Contact: Rachael Schmidt
Questions?

jessica.maxwell@unmc.edu