Surgical Treatment of Breast Cancer

Doreen M. Agnese, MD
Associate Professor
Department of Surgery
Division of Surgical Oncology
The Ohio State University Wexner Medical Center

Screening and Diagnosis
Patient presentations

- Asymptomatic
  - Abnormal mammogram
- Symptomatic
  - Palpable mass
  - Changes in the skin of the breast/nipple
  - Nipple discharge
  - Axillary mass

Screening Guidelines, general population

- Clinical encounter about every three years for women in their 20s-30s, and annually for women ≥ 40
- Annual screening mammogram beginning at age 40 (tomosynthesis)
- Breast awareness

Spiculated mass

Suspicious microcalcifications
# Symptomatic patients

- Evaluate with complete history and physical examination
- Diagnostic imaging
  - Bilateral mammogram, even if unilateral symptoms
  - May use other imaging modalities
    - Ultrasound
    - MRI

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Cystic lesion, requires no further therapy
Solid mass with features suspicious for malignancy

MRI

Enhancing mass, suspicious
### Methods of Diagnosis

- **Palpable lesion**
  - fine needle aspiration (FNA)
  - Core/Tru-cut biopsy
  - excisional biopsy

- **Nonpalpable lesion**
  - stereotactic biopsy
  - ultrasound-guided core needle biopsy
  - imaging localized excisional biopsy

- **Abnormal skin—punch biopsy**
Stereotactic Breast Biopsy

- Prone position with breast through opening in table
- Mammographic views in different positions
- Target lesion in 3 coordinates
- Post biopsy image to confirm sampling

Ultrasound-Guided Core or MammoTomate Biopsy
Non-invasive breast cancer

DCIS

- Usually presents as an abnormal mammogram with clustered calcifications
- Nodal metastases are rare (1%), likely associated with unrecognized microinvasion
- Up to ½ of recurrences are invasive
Management

• Treatment → lumpectomy with radiation therapy (negative margins) or total mastectomy
• Evaluation of the axillary lymph nodes is generally not necessary (unless mastectomy)

Invasive cancers
Invasive breast cancer

- Most common type is infiltrating ductal (75%)
- Less common variants of ductal
  - Medullary (6%)-better prognosis
  - Tubular (2%)-excellent prognosis
  - Colloid (1-2%)-better prognosis
- Invasive lobular (10%)
  - Indistinct margins, extensive infiltration
  - Harder to detect mammographically
  - Significant incidence of multicentricity

Surgical Management of Invasive Breast Cancer

- Breast (removal of primary tumor)
  - total mastectomy
  - lumpectomy (breast conservation) plus radiation therapy
- Axillary lymph nodes (staging evaluation)
  - axillary node dissection
  - sentinel lymph node mapping and biopsy
### Partial mastectomy/ lumpectomy

**Segmental**

*Author: National Cancer Institute/Linda Bartlett (Photographer)*

### Contraindications to Breast Conservation

- Large tumors or large tumor: breast ratio
- Multicentric disease
- Extensive DCIS
- Indeterminant mammographic findings elsewhere in breast
- Previous breast radiation
- Autoimmune disorders affecting skin: scleroderma (contraindication to RT)
Total (simple) mastectomy

A. Tissue in pink is removed. This represents all breast tissue
• No effort is made to remove axillary lymph nodes
• Can be used for treatment or prophylaxis

Skin-sparing mastectomy

• “Keyhole” incision (skin preserved)
• Tissue removed at mastectomy
• Allows for more natural reconstruction by preserving breast envelope
**NSM/ASM**

- Combines skin sparing mastectomy with preservation of nipple and/or areola
- Role for therapy and prophylaxis unclear
  - Historic rates of nipple involvement in the setting of cancer range from 0-58%
  - 316 consecutive mastectomy specimens (232 therapeutic, 84 prophylactic) evaluated
    - 71% of therapeutic had no path abnormality, 21% had DCIS and 8% had LCIS
    - None of the prophylactic mastectomies had nipple involvement by DCIS or invasive carcinoma

Brachtel, *JCO* 2009; 27(30): 4948

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**NSABP B-06**

- There is no difference in disease-free, distant disease-free or overall survival between mastectomy and lumpectomy.

- The addition of radiation to lumpectomy is important in decreasing the risk of local recurrence.
Nodal assessment

- Sentinel lymph node biopsy current standard
- Axillary node dissection if sln pos or can’t be identified
  - Higher risk of lymphedema (25% vs 5%)
  - Higher likelihood of nerve injury
  - More mobility issues

Sentinel Lymph Node Biopsy
Management of Positive SLN

- Previously, completion node dissection in all cases
- Currently, completion node dissection still standard for patients treated with mastectomy
- Certain patients treated with BCT may be able to avoid completion node dissection

ACOSOG Z11

Source: American Society of Clinical Oncology (https://www.asco.org/)
### Clinical Implications

In clinically node-negative patients undergoing BCT with macrometastases in the SN:

- Systemic Rx decision made
- ALND not necessary for local control
- ALND does not contribute to survival

### Reconstruction Options/Issues Following Mastectomy

- Skin-sparing procedures
- Saline tissue expanders / saline implants
- Tissue transfer procedures
  - DIEP flap
  - TRAM or other rotational flaps
- Immediate versus delayed reconstruction
**Locally advanced breast cancers**

- Large tumor (>5cm) or skin changes (edema, ulceration, chest wall fixation) or fixed axillary lymph nodes
- Account for 10-15% of breast cancer in US, higher in developing countries
- Best results with neoadj chemo, followed by surgery with adjuvant RT as needed

**Inflammatory breast cancers**

- Account for <3% of breast cancers
- Characterized by brawny induration, erythema, and edema of the skin (peau d’orange)
- Dermal lymphatic involvement seen on skin biopsy
- May be mistaken for bacterial infection
Inflammatory breast cancer

- Distant metastasis is present in about 25% at presentation
- Neoadjuvant chemo may affect dramatic regression
- After chemo, MRM is performed
- Adjuvant chemo is often given
- RT to chest wall, supraclav, IM and axillary nodal basins is also given
- 5-yr survival rates approach 30%

Complications of local therapy
Angiosarcoma

Lymphedema

Author: Medical doctors  CC BY-SA 4.0
The Systemic Approach to Breast Cancer

Raquel E. Reinbolt, MD
Division of Medical Oncology
The Stefanie Spielman Comprehensive Breast Center
The Ohio State University Comprehensive Breast Center

Learning Objectives:

- To review breast cancer systemic therapy approaches for early stage, locally advanced, and (briefly) metastatic breast cancer
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- To review breast cancer systemic therapy approaches for early stage, locally advanced, and (briefly) metastatic breast cancer
- To review principles of survivorship

Stages of Breast Cancer

<table>
<thead>
<tr>
<th>Localized Disease:</th>
<th>Metastatic Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Distribution - 60%</td>
<td>• Distribution 5-7%</td>
</tr>
<tr>
<td>• 5-Year Survival – 99%</td>
<td>• 5-year survival 26%</td>
</tr>
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</table>

Locally Advanced

- Distribution 32%
- 5-year Survival 85%

Based on Surveillance Epidemiology and End Result Database

Cancer Research UK / Wikimedia Commons
Not All Breast Cancer Is The Same

Breast Cancer → Hormone Receptor (+) 65-75% → HER2+ 15-20% → TN* 15% *Triple Negative

Early Stage Breast Cancer

Excellent Prognosis!
Most individuals diagnosed with breast cancer today have early stage disease, and after the institution of proper treatment, have a low chance of recurrence
Primary Therapies: Early Stage Disease

- Surgery
- Radiation
- Systemic therapies

Systemic Therapy Selection Factors

- Lymph node involvement
- Tumor size
- Tumor grade
- Lymphovascular invasion
- Ki-67 (proliferation)
- Patient age and co-morbidities
- ER, PR, Her-2 → Targeted therapy
Treating & Targeting ER+ Breast Cancer

Hormone Positive Disease

Question:
Is chemotherapy required prior to surgery in hormone positive disease?

Answer: It depends!
Answer: Yes!
Plan: Neoadjuvant Chemotherapy

1st Chemotherapy
2nd Surgery
3rd +/- Radiation
4th +/- Endocrine Therapy
• TAM vs AI
• Possible Zoladex (GnRH agonist)

Answer: No!
Plan: Adjuvant Chemotherapy, If Needed

1st Surgery
2nd Chemotherapy
3rd +/- Radiation
4th +/- Endocrine Therapy
• TAM vs AI
• Possible Zoladex (GnRH agonist)
How to Determine Benefit of Chemotherapy In Node Negative Patients After Surgery:
Gene Expression Assays

• Predict benefit of chemotherapy
• Predict likelihood of distant breast cancer recurrence by placing patient into a risk category

Chemo or No Chemo?

• 56yo F with a 2cm invasive ductal carcinoma, node negative
• ER 70% PR 0% HER2 negative
• Oncotype reveals a recurrence score of 36

>30 = HIGH RISK!
Benefit!

- Regimens for consideration:
  - Adriamycin/Cytoxan + Taxol
  - Taxotere/Cytoxan

**Treatment Plan:**
**AC & T (Dose Dense)**

<table>
<thead>
<tr>
<th>Adriamycin &amp; Cytoxan (AC)</th>
<th>Taxol (T)</th>
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<tbody>
<tr>
<td>- Every 2 weeks, 4 times (cycles)</td>
<td></td>
</tr>
<tr>
<td>- Total of 8 weeks of therapy</td>
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<tr>
<td>- TTE</td>
<td></td>
</tr>
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<td>- Growth Factor</td>
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<td></td>
<td>- Total of 8 weeks of therapy</td>
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<tr>
<td></td>
<td>- Growth Factor</td>
</tr>
<tr>
<td></td>
<td>16 weeks total of therapy</td>
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</table>
### Treatment Plan: AC & T (Weekly)

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<td></td>
</tr>
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20 weeks total of therapy

### Treatment Plan: TC

<table>
<thead>
<tr>
<th>Taxotere &amp; Cytoxan (TC)</th>
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<tbody>
<tr>
<td>• Every 3 weeks, 4 times (cycles)</td>
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<tr>
<td>• Total of 12 weeks of therapy</td>
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<tr>
<td>• +/- Growth Factor</td>
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Total 12 weeks of therapy
What About Hormone Positive, Lymph Node Positive Patients?

- Discussion of chemotherapy
  - Consideration of age, other comorbidities
  - Number of nodes positive

- 1-3 lymph nodes positive:
  - Potential role for gene expression testing

The Addition of GnRH Agonist Therapy

Can we maximize anti-estrogen therapy?
**Endocrine Therapy**

- **Have to assess menopausal status prior to therapy (chemotherapy or endocrine therapy)!**

- **Pre-menopausal:** Tamoxifen (TAM) x 10yrs; TAM/AI + ovarian suppression
  - Side effects:
    - Thromboembolic events
    - Endometrial cancer
    - Hot flashes, vaginal symptoms
    - Important to discuss birth control use while on this med!

- **Post-menopausal:** Aromatase inhibitor (AI)
  - 5yrs vs 10 yrs
  - Letrozole (Femara), Anastrozole (Arimidex), Exemestane (Aromasin)
  - Superior to Tamoxifen in this population; none superior to another
  - Can use after 2-5yrs of Tamoxifen
  - Side effects:
    - Mylagias/arthritis is the major reason for discontinuation
    - Osteoporosis- everyone gets calcium/vit D; should get bone density prior to treatment and every 2yrs
Treating & Targeting
Triple Negative
Breast Cancer

Triple Negative Disease

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CHEMOTHERAPY
### TNBC: Neoadjuvant vs Adjuvant: Timing

<table>
<thead>
<tr>
<th>Neoadjuvant</th>
<th>Adjuvant</th>
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<tbody>
<tr>
<td>Optimization of surgical margins</td>
<td>Complete staging</td>
</tr>
<tr>
<td>Real time monitoring of disease response</td>
<td></td>
</tr>
<tr>
<td>pCR and prognostication</td>
<td></td>
</tr>
<tr>
<td>Associated with improvement in Disease Free Survival (DFS)</td>
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### TNBC: Neoadjuvant vs Adjuvant: Regimen Selection

- **Standard Regimens:**
  - anthracycline + alkylating agent + taxane

- **How about Platinum agents?**
  - Must balance additional toxicity added from therapy with potential benefit, particularly in patients with locally advanced disease
## TNBC: Other Therapy Thoughts

- What about residual disease after neoadjuvant chemotherapy?
  - No proven role for continuing systemic therapy
  - Possible time to consider trials
  - Additional data to come
  - Surveillance is key!

## How can we target TNBC?

- Platinum chemotherapy
- PARP Inhibitors
- Immunotherapy
- Androgen receptor blockers
- Genomic profiling of tumors
HER2+ Breast Cancer

*HER2* (human epidermal growth factor receptor 2):
- Gene that may play a role in breast cancer development
- Breast cancers with *HER2* gene amplification or *HER2* protein overexpression benefit from HER2-targeted therapy
- HER2 Antibodies = Trastuzumab & Pertuzumab
  - Bind to different domains of the HER2 receptor
**HER2+ Neoadjuvant Chemotherapy**

*Consider if a Stage II or > (2cm and above or node positive)*

*Use dual-HER2 targeted therapy with Trastuzumab & Pertuzumab combined with chemotherapy*

1. Chemotherapy
   - + HER2 targeted therapy
2. Surgery
3. +/- Radiation
4. Herceptin +/- Endocrine Therapy
   - Complete 1 year total of Herceptin
   - TAM vs AI
   - Possible Zoladex (GnRH agonist)

**HER2+ Adjuvant Chemotherapy**

*Consider if a Stage I*

*Ongoing studies to minimize amount of concurrent chemotherapy given in this population*

1. Surgery
2. Chemotherapy
   - + HER2 targeted therapy
3. +/- Radiation
4. Herceptin +/- Endocrine Therapy
   - Complete 1 year total of Herceptin
   - TAM vs AI
   - Possible Zoladex (GnRH agonist)
### Early Stage Disease: Survivorship

- H&P: more frequent after initial diagnosis
- Patient education on recurrence signs/symptoms
- Genetic counseling
- Breast self-exam
- Mammography
- Pelvic examinations - especially while on TAM
- Awareness of therapy-specific sequelae
- **Not recommended:** routine bloods tests, tumor markers, imaging (outside of breast imaging)

### Metastatic Breast Cancer...

A Few Thoughts
**Metastatic Breast Cancer**

- Approximately 40,000 new cases per year in the United States
- **Pattern of metastases:**
  - Bone
  - Axillary/Mediastinal lymph nodes
  - Lungs
  - Liver
  - Brain (Triple Negative; HER2+)
  - Mucous membranes (Invasive Lobular Carcinoma)
- **Survival:**
  - Average 3 years

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**INITIAL CONSIDERATIONS FOR NEWLY DIAGNOSED METASTATIC BREAST CANCER**

- **Confirmation of Diagnosis**
  - Biopsy metastatic lesion if possible; consider genomic profiling!
  - Re-test hormone receptor and HER2 over expression
- **Complete Staging**
  - CT scans of chest, abdomen and pelvis
  - Bone scan
  - PET/CT (alternative to CT and bone scans)
  - Use of tumor markers (CA 15-3, CA 27.29, CEA)- ???
INITIAL CONSIDERATIONS FOR NEWLY DIAGNOSED METASTATIC BREAST CANCER

- Therapeutic Goals: **INCURABLE DISEASE:**
  - Palliation of cancer related symptoms.
  - **Quality of life is the key!**
  - Prolongation of survival; however, increased response rates do not necessarily correlate with improvement in survival

Metastatic Breast Cancer

- A Word On Therapy Selection
  - “Pace” of disease
  - Location
  - Targeted approach still applies
  - Performance status
  - Clinical trials!
## Conclusions

- There are about 230,000 new cases of breast cancer in the United States each year (about 40,000 new cases of metastatic breast cancer)

- Treatment of breast cancer is complex and depends on multiple factors and patient preference

- New approaches to breast cancer treatment that take advantage of breast cancer biology ("targeted" approaches) are being developed with increased frequency

- Survivorship programming is essential