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

Symptomatic patients

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

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

**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

**Methods of Diagnosis**
- Palpable lesion
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**MRI**
Enhancing mass, suspicious
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 Mammotome 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

Contraindications to Breast Conservation

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

Total (simple) mastectomy

- 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

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

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

ACOSOG Z11

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

- To review breast cancer systemic therapy approaches for early stage, locally advanced, and (briefly) metastatic breast cancer
Learning Objectives:

• 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

Localized Disease:
• Distribution - 60%
• 5-Year Survival – 99%

Locally Advanced
• Distribution 32%
• 5-year Survival 85%

Metastatic Disease
• Distribution 5-7%
• 5-year survival 26%

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

Hormone Positive Disease

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

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

1. Chemotherapy
2. Surgery
3. +/- Radiation
4. +/- Endocrine Therapy
   - TAM vs AI
   - Possible Zoladex (GnRH agonist)

Answer: No!
Plan: Adjuvant Chemotherapy, If Needed

1. Surgery
2. Chemotherapy
3. +/- Radiation
4. +/- 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 (Weekly)
- Adriamycin & Cytoxan (AC)
  - Every 2 weeks, 4 times (cycles)
  - Total of 8 weeks of therapy
  - TTE
  - Growth Factor
- Taxol (T)
  - Every week, 12 times (cycles)
  - Total of 12 weeks of therapy
  - 20 weeks total of therapy

Treatment Plan: AC & T (Dose Dense)
- Adriamycin & Cytoxan (AC)
  - Every 2 weeks, 4 times (cycles)
  - Total of 8 weeks of therapy
  - TTE
  - Growth Factor
- Taxol (T)
  - 16 weeks total of therapy

Treatment Plan: TC
- Taxotere & Cytoxan (TC)
  - Every 3 weeks, 4 times (cycles)
  - Total of 12 weeks of therapy
  - +/- Growth Factor
  - 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!

Endocrine Therapy

- 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

TNBC: Neoadjuvant vs Adjuvant: Timing

- Neoadjuvant
  - Optimization of surgical margins
  - Real time monitoring of disease response
  - pCR and prognostication
  - Associated with improvement in Disease Free Survival (DFS)

- Adjuvant
  - Complete staging

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

Treating & Targeting 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+ Breast Cancer
**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*

<table>
<thead>
<tr>
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**HER2+ Adjuvant Chemotherapy**

*Consider if a Stage I*

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

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**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

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 overexpression
- 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)- ???

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
- 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