

# **Surgical Treatment of Breast Cancer**

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## **Screening and Diagnosis**

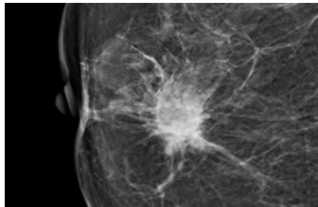
### **Patient presentations**

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

### **Screening Guidelines, general population**

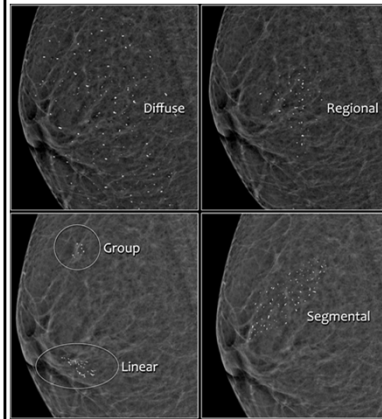
- Clinical encounter about every three years for women in their 20s-30s, and annually for women  $\geq 40$
- Annual screening mammogram beginning at age 40 (tomosynthesis)
- Breast awareness

NCCN Guidelines, version 2.2016



Source: The Radiology Assistant

**Spiculated mass**

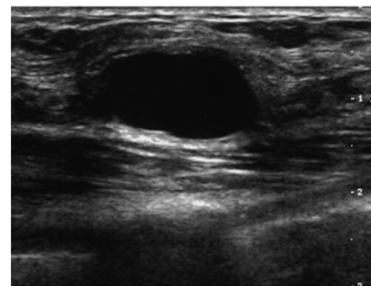


Source: The Radiology Assistant

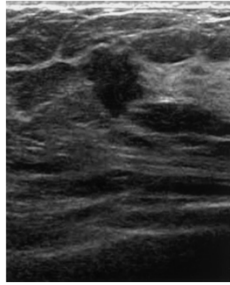
**Suspicious  
microcalcifications**

## Symptomatic patients

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

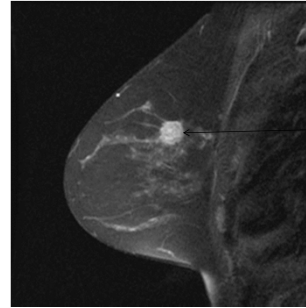


**Cystic lesion, requires no further therapy**



**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

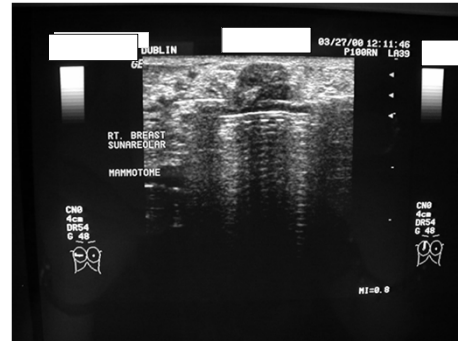
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## Stereotactic Breast Biopsy

- 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 1/2 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

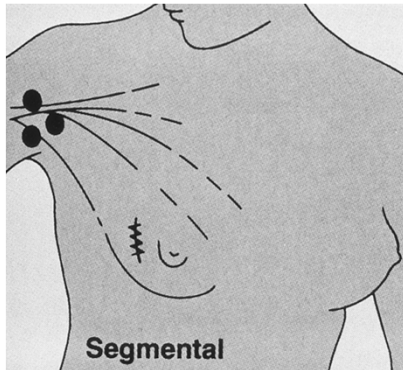
### Invasive breast cancer

- 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

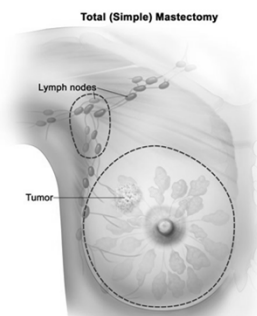


Author: National Cancer Institute/Linda Bartlett (Photographer)

## 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



Author: National Cancer Institute

- 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

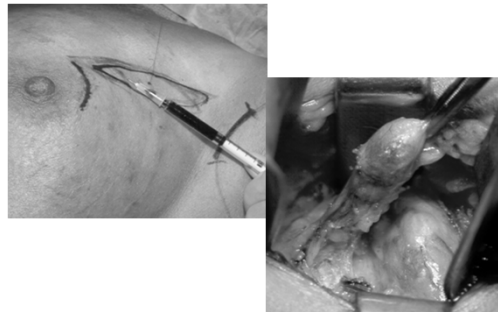
## NSABP B-06

- 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

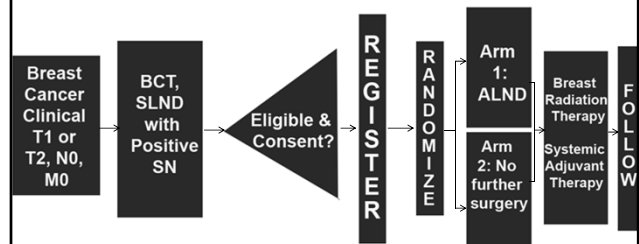
## Sentinel Lymph Node Biopsy



## 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**

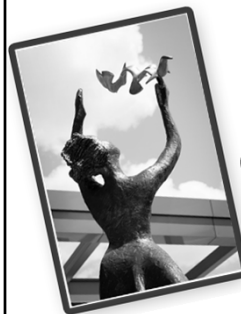
- Large tumor (>5cm) or skin changes (edema, ulceration, chest wall fixation) or fixed axillary lymph nodes
- Account for 10-15% of breast cancer in US, higher in developing countries
- Best results with neoadj chemo, followed by surgery with adjuvant RT as needed

### **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

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Division of Medical Oncology  
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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

### Localized Disease:

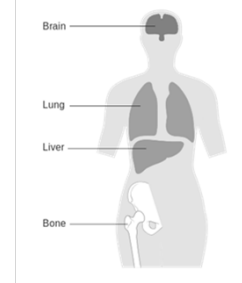
- Distribution - 60%
- 5-Year Survival – 99%

### Metastatic Disease

- Distribution 5-7%
- 5-year survival 26%

### Locally Advanced

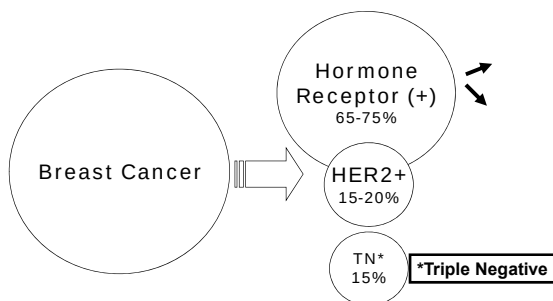
- Distribution 32%
- 5-year Survival 85%



Based on Surveillance Epidemiology and End Result Database

Cancer Research UK / Wikimedia Commons

## Not All Breast Cancer Is The Same



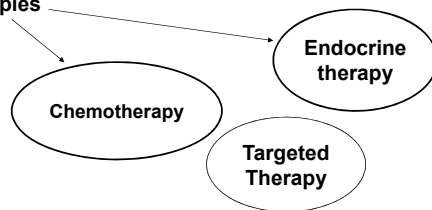
## Early Stage Breast Cancer

### *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

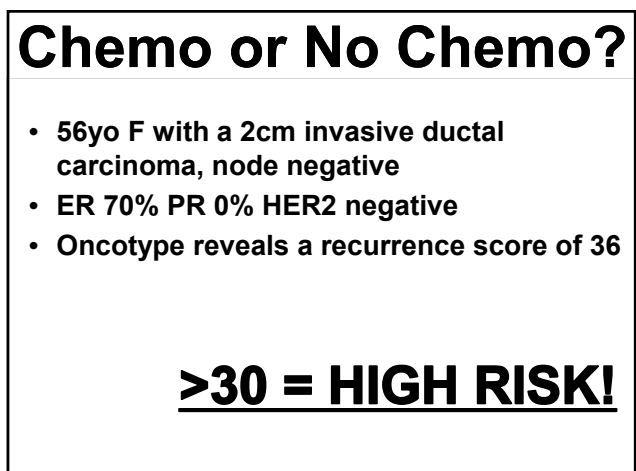
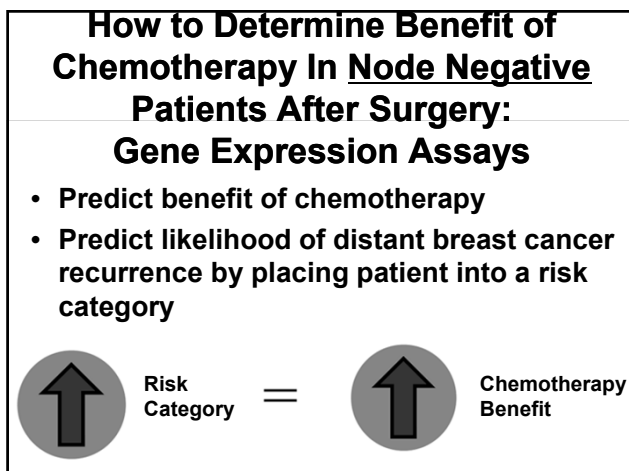
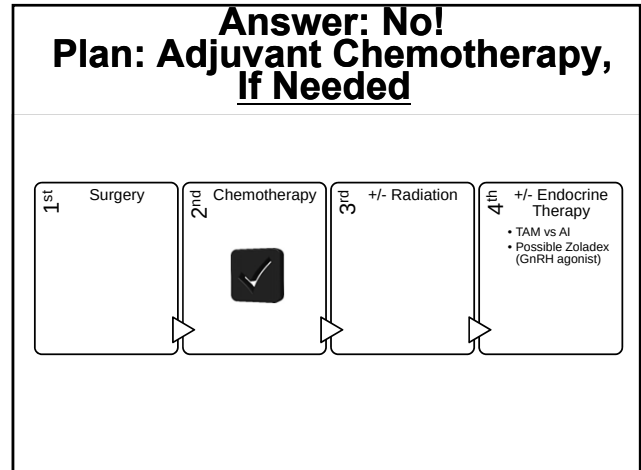
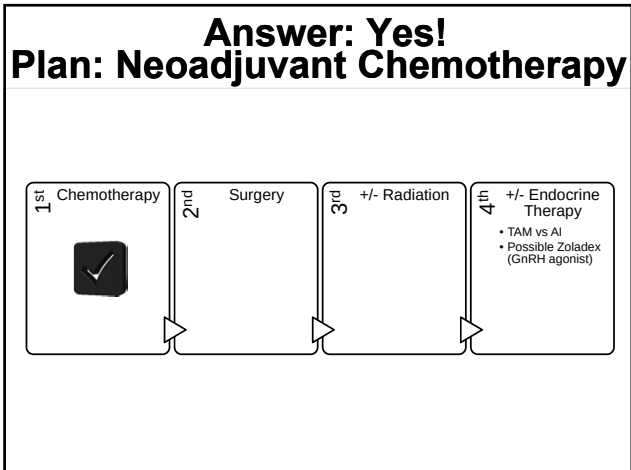
## Hormone Positive Disease

### Question:

Is chemotherapy required prior to surgery in hormone positive disease?

Answer: It depends!





C H E M O T H E R A P Y

## Benefit!

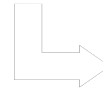
- **Regimens for consideration:**

- **Adriamycin/Cytoxan + Taxol**
- **Taxotere/Cytoxan**

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

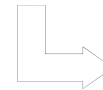
Adriamycin  
& Cytoxan  
(AC)

- Every 2 weeks, 4 times (cycles)
- Total of 8 weeks of therapy
- TTE
- Growth Factor



Taxol  
(T)

- Every 2 weeks, 4 times (cycles)
- Total of 8 weeks of therapy
- Growth Factor

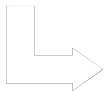


16 weeks  
total of  
therapy

### Treatment Plan: AC & T (Weekly)

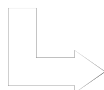
Adriamycin  
& Cytoxan  
(AC)

- 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

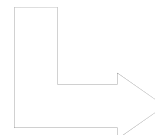


20 weeks  
total of  
therapy

### Treatment Plan: TC

Taxotere &  
Cytoxan  
(TC)

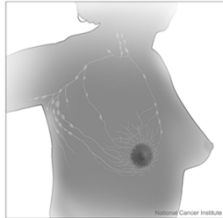
- Every 3 weeks, 4 times (cycles)
- Total of 12 weeks of therapy
- +/- Growth Factor



Total 12  
weeks of  
therapy

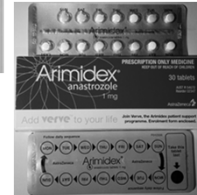
## What About Hormone Positive, Lymph Node Positive Patients?

- 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:
    - Myalgias/arthralgias 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**

**≡**

**CHEMOTHERAPY**

**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

• Cortazar P, Zhang L, Untch M, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet 2014;384(9938): 164-72.  
 • Liedtke C, Mazouni C, Hess KR, et al. Response to neoadjuvant therapy and long-term survival in patients with TNBC. J Clin Oncol 2008; 26:1276.  
 • von Minckwitz G, Untch M, Blohmer JU, et al. Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes J Clin Oncol 2012;30:1796.

**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



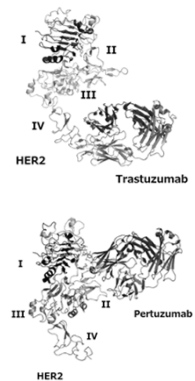
## Treating & Targeting HER2+ Breast Cancer



## HER2+ Breast Cancer

**HER2** (human epidermal growth factor receptor 2):

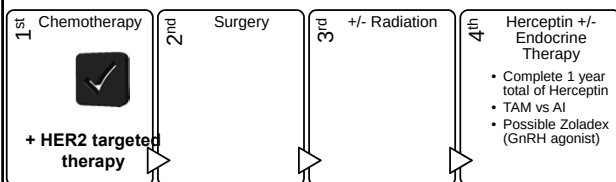
- Gene that may play a role in breast cancer development
- Breast cancers with *HER2* gene amplification or *HER2* protein overexpression benefit from HER2-targeted therapy
- HER2 Antibodies =
  - Trastuzumab & Pertuzumab
  - Bind to different domains of the HER2 receptor



## HER2+ Neoadjuvant Chemotherapy

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

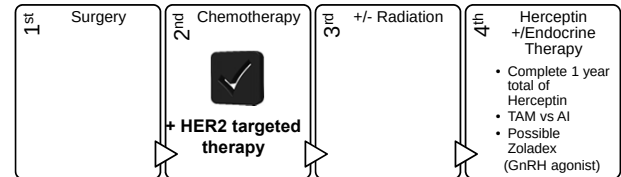
\*Use dual-HER2 targeted therapy with Trastuzumab & Pertuzumab combined with chemotherapy



## HER2+ Adjuvant Chemotherapy

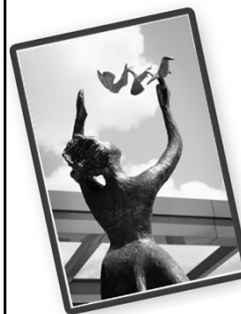
\*Consider if a Stage I

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



## 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

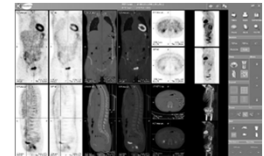
- Confirmation of Diagnosis
  - Biopsy metastatic lesion if possible; consider genomic profiling!
  - Re-test hormone receptor and HER2 over expression
- Complete Staging
  - CT scans of chest, abdomen and pelvis
  - Bone scan
  - PET/CT (alternative to CT and bone scans)
  - Use of tumor markers (CA 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 years (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**