



Surgical treatment of breast cancer

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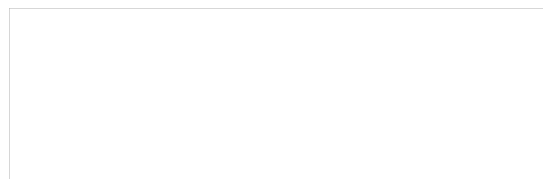
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Screening and
Diagnosis

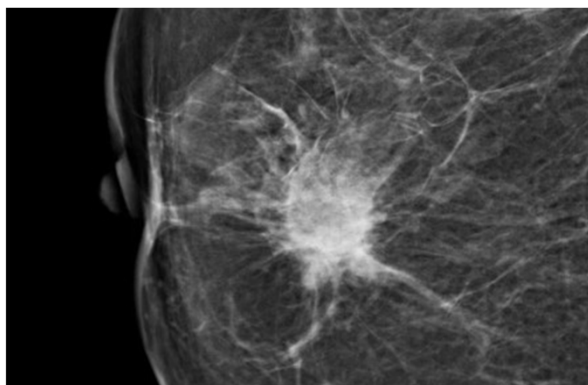


Patient presentations

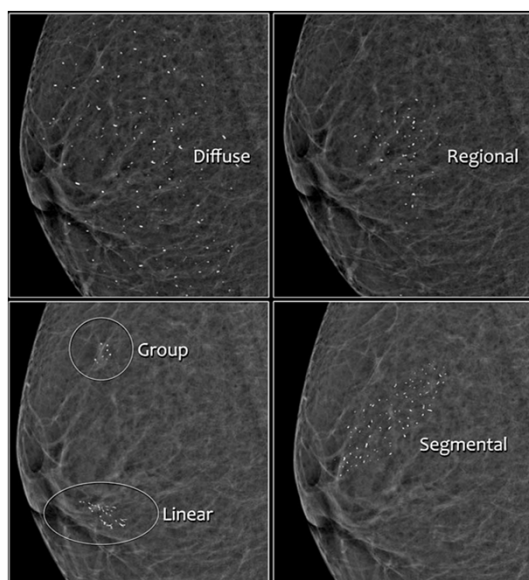
- Asymptomatic
 - Abnormal mammogram
- Symptomatic
 - Palpable mass
 - Changes in the skin of the breast/nipple
 - Nipple discharge
 - Axillary mass

Screening Guidelines, general population

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



Spiculated mass

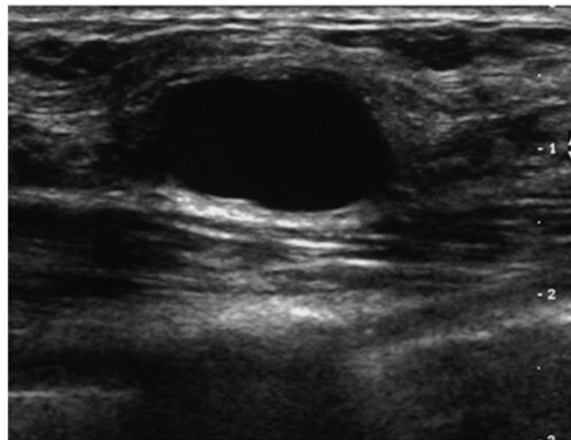


Suspicious microcalcifications

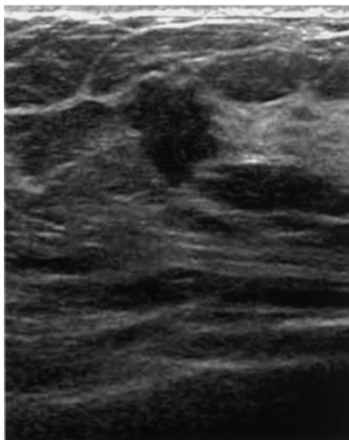
Symptomatic patients

- 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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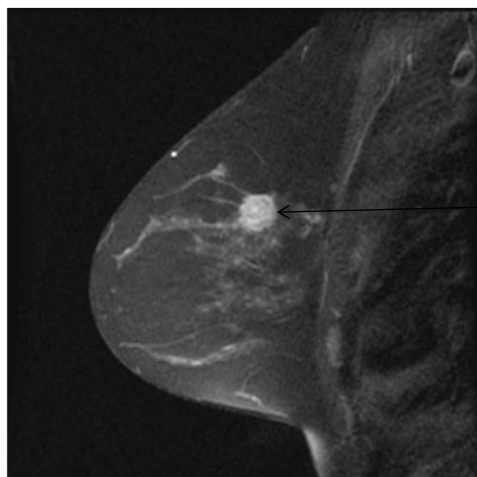


Cystic lesion, requires no further therapy



Solid mass with features suspicious for malignancy

MRI

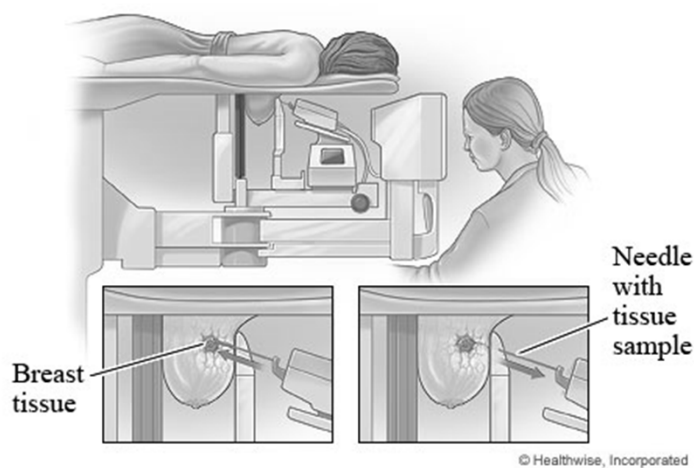


Enhancing mass, suspicious

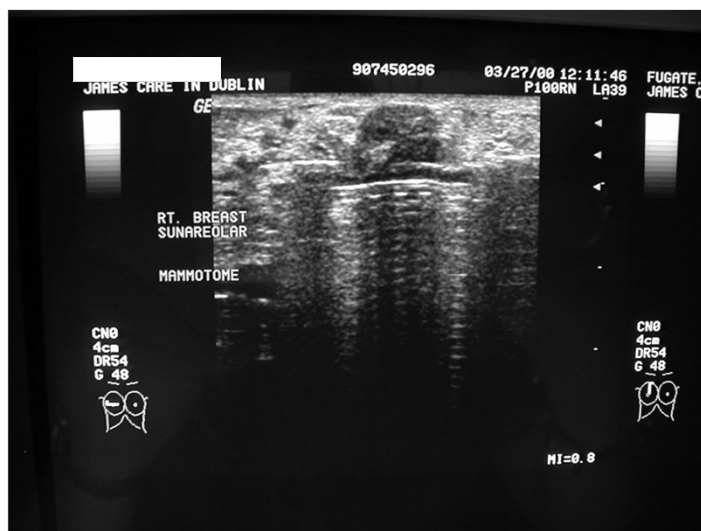
Methods of Diagnosis

- 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



Ultrasound-Guided Core or Mammotome Biopsy



Non-invasive breast cancer

DCIS

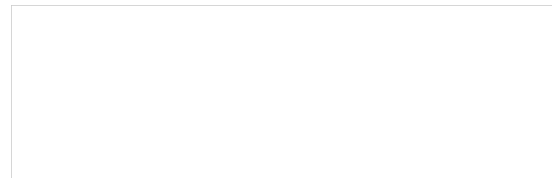
- Usually presents as an abnormal mammogram with clustered calcifications
- Nodal metastases are rare (1%), likely associated with unrecognized microinvasion
- Up to 1/2 of recurrences are invasive

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



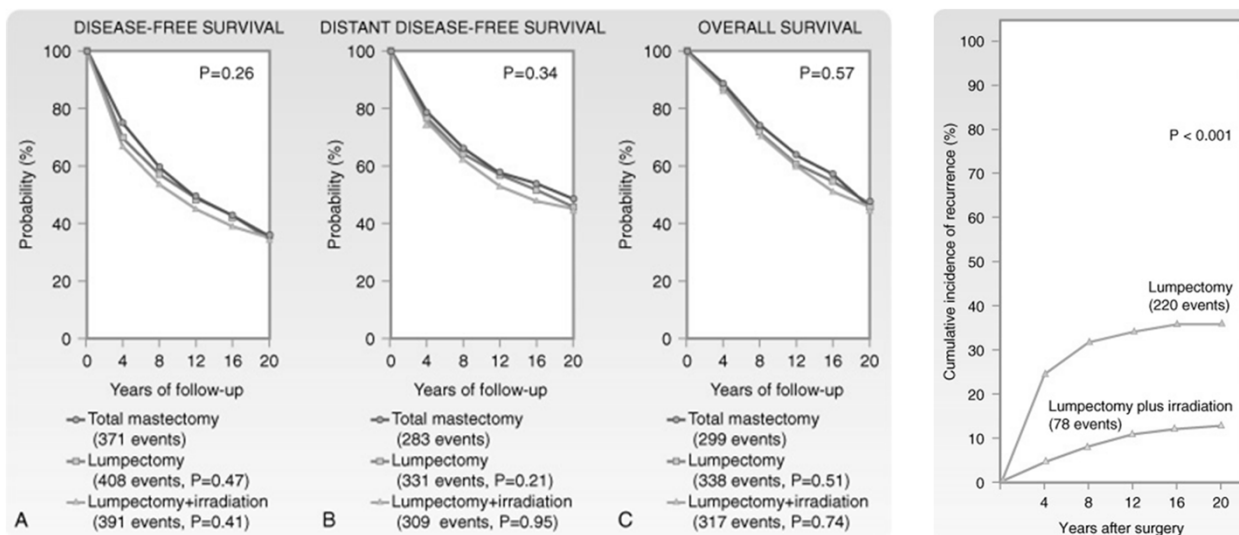
Invasive breast cancer

- 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

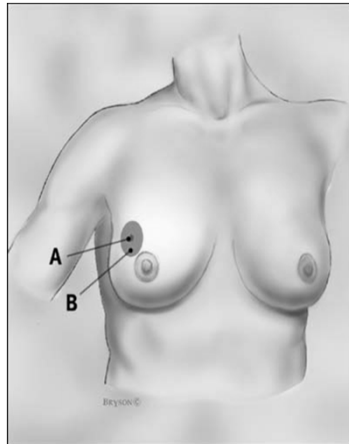
Surgical Management of Invasive Breast Cancer

- 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

NSABP B-06



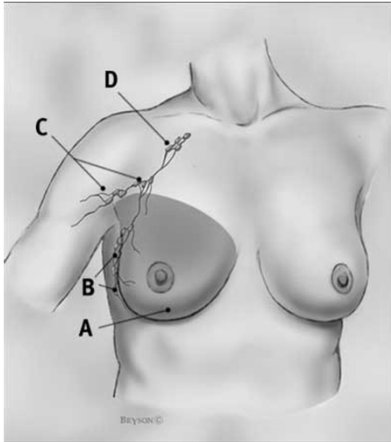
Partial mastectomy/ lumpectomy



Contraindications to Breast Conservation

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

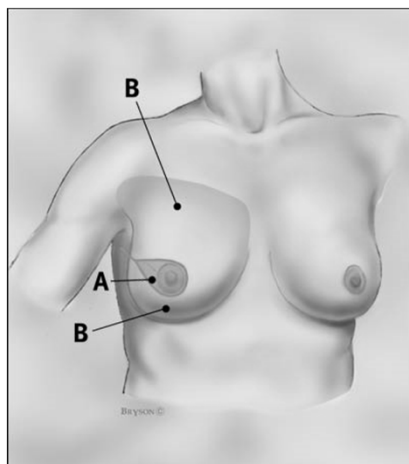
Total (simple) mastectomy



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

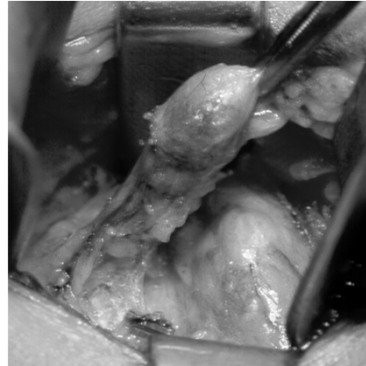
NSM/ASM

- Combines skin sparing mastectomy with preservation of nipple and/or areola
- Appropriate when nipple is not involved with cancer or atypical cells.
- Usually involves incision in inframammary fold with preservation of entire skin envelope.
- Most appropriate in breasts without ptosis as nipple can not be repositioned.

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

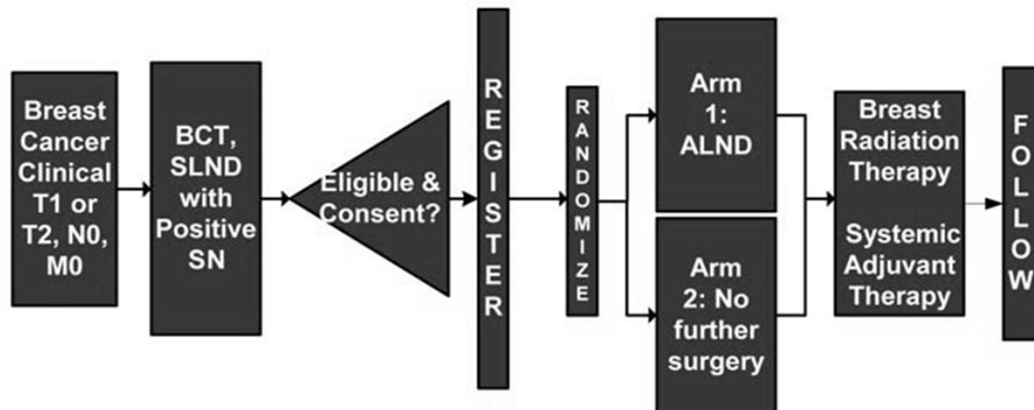
Sentinel Lymph Node Biopsy



Management of Positive SLN

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

ACOSOG Z11



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

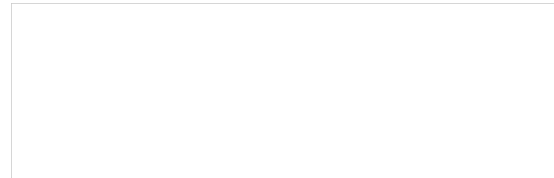
- Account for <3% of breast cancers
- Characterized by brawny induration, erythema, and edema of the skin (peau d'orange)
- Dermal lymphatic involvement seen on skin biopsy
- May be mistaken for bacterial infection

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%



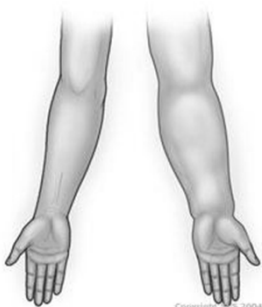
Complications of
local therapy



Angiosarcoma



Lymphedema



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Systemic Therapy for Breast Cancer

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Learning Objectives

- ☐ To Review Breast Cancer Basics
- ☐ To Review Systemic Therapy of Breast Cancer
- ☐ To Review Approved Indications for Immunotherapy in Breast Cancer

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Breast Cancer Basics

Breast Cancer Basics: Stats

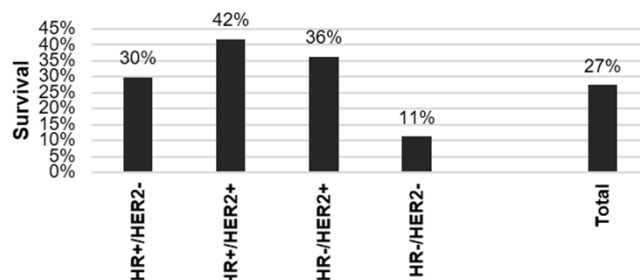
- **Incidence:** In 2022, there will be an estimated 290,560 new cases of breast cancer with 43,780 deaths

- 2nd most common cause of death in women

- **De novo Metastatic:** 5% of cases are metastatic at diagnosis

	Women	Men
New Cases	287,850	2,710
Deaths	43,250	530
Lifetime Risk	1 in 8 women	1 in 833 men

5 year Survival in Metastatic Breast Cancer



Siegel et al. Ca Cancer j Clin. 2022.

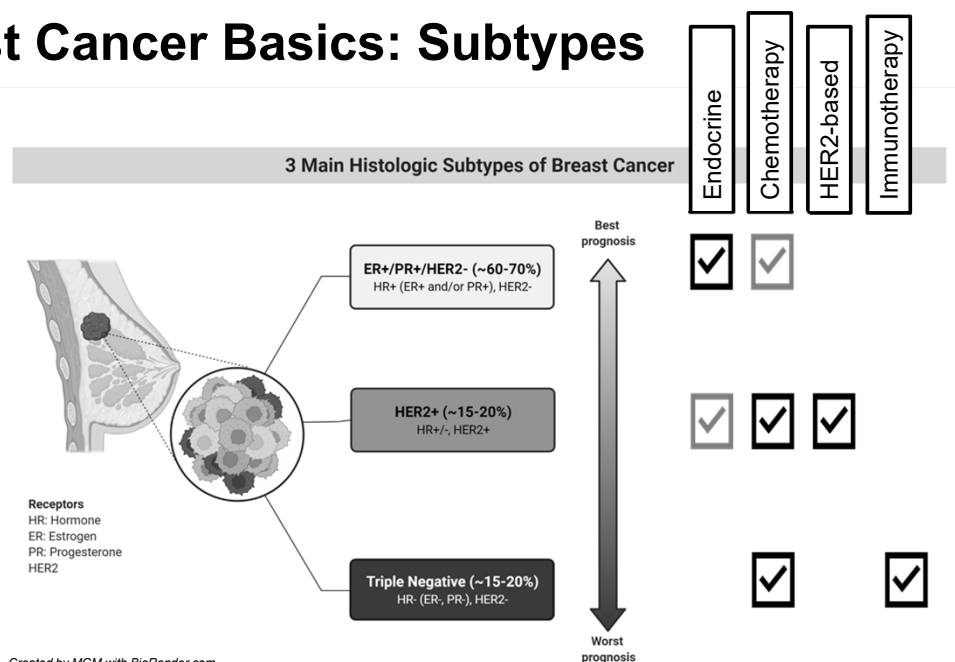
Malmgren et al. Breast Cancer Res Treat. 2018.

Howlander et al. CEBP. 2018.

It's All About the Receptors

- Breast Cancers are typically tested for 3 main receptors
 - Estrogen Receptor (ER)
 - Progesterone Receptor (PR)
 - Human Epidermal Growth Factor Receptor 2 (HER2)
- The presence (or absence) of these receptors determines:
 - Clinical Outcomes
 - Systemic Treatment
 - Timing of treatment
 - Type of treatment
 - Duration of treatment

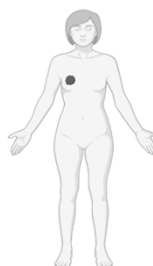
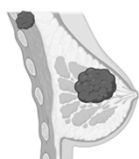
Breast Cancer Basics: Subtypes



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The Pillars of Early Breast Cancer Treatment

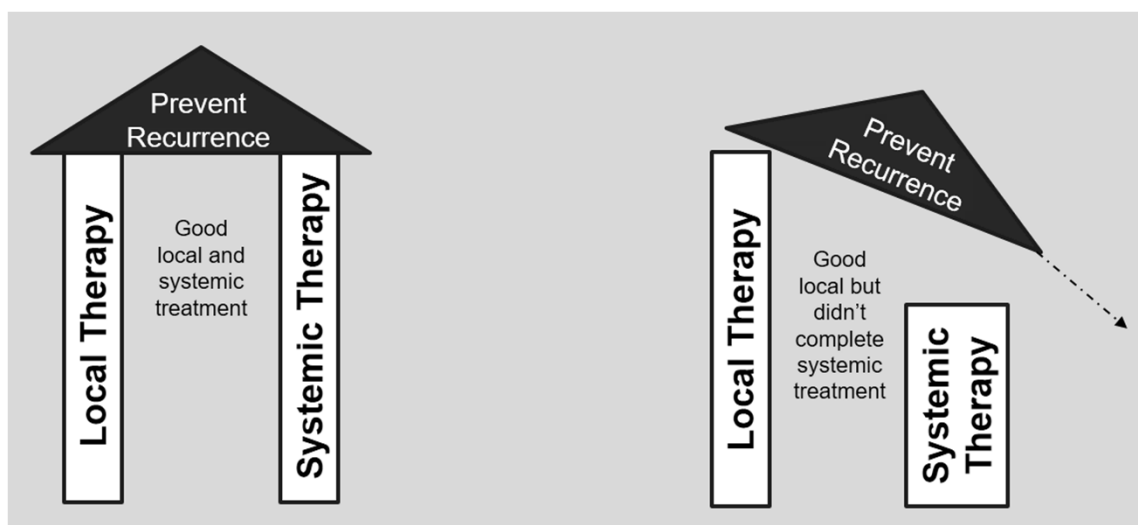
Local Therapy	Systemic Therapy
<ul style="list-style-type: none"> Breast Surgery and Nodal Evaluation <ul style="list-style-type: none"> Mastectomy vs lumpectomy Sentinel node vs axillary node dissection Radiation 	<ul style="list-style-type: none"> Neoadjuvant or Adjuvant <ul style="list-style-type: none"> Chemotherapy HER2-Base Therapy Immunotherapy Endocrine therapy



Created by MGM with BioRender.com

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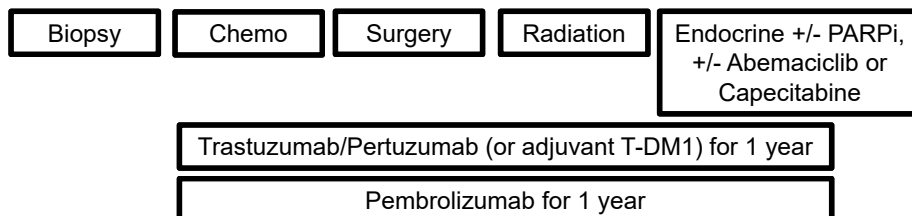
The Pillars of Breast Cancer Treatment



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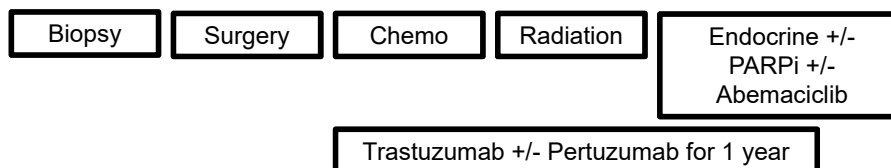
Systemic Therapy

Neoadjuvant (before surgery) Breast Cancer Treatment



- **Who gets neoadjuvant chemotherapy?**
 - Triple Negative Breast Cancer $\geq 1\text{cm}$ or + lymph nodes
 - HER2+ Breast Cancer $\geq 2\text{cm}$ or + lymph nodes
 - Some ER+ Breast Cancer
- Can be followed by adjuvant therapy after surgery
 - Some agents will span both neoadjuvant and adjuvant settings

Adjuvant (after surgery) Breast Cancer Treatment



- **Who gets adjuvant chemotherapy?**
 - Triple Negative Breast Cancer, $< 1\text{cm}$ and no lymph nodes
 - HER2+ Breast Cancer, $< 2\text{cm}$ and no lymph nodes
 - Some ER+ breast cancer, Oncotype $\geq 26^*$
- **Who can be spared chemotherapy?**
 - Most ER+ patients
 - Some small ($< 5\text{mm}$), node negative triple negative or HER2+ breast cancers

Multigene Assays Help with Risk Recurrence Estimates

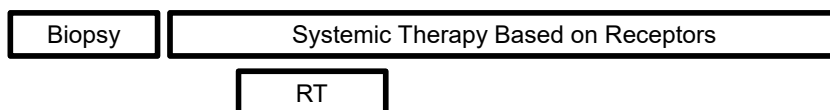
	Oncotype (preferred)	MammaPrint
No. Genes	21 genes	70 genes
Predictive	YES	Unknown
Prognostic	YES	YES
Result Range	0 to 100 [0 to 11 = Stage 1A] [0 to 25*, no chemo] [26+, chemo]	Low [no chemo] High [chemo]

**Premenopausal patients with oncotype score 18 to 25, consider ovarian suppression and/or chemotherapy*

ALL patients with ER+ breast cancer will receive 5 to 10 years of endocrine therapy (Tamoxifen or an aromatase inhibitor like anastrozole, letrozole, or exemestane)

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Metastatic (advanced) Breast Cancer Treatment

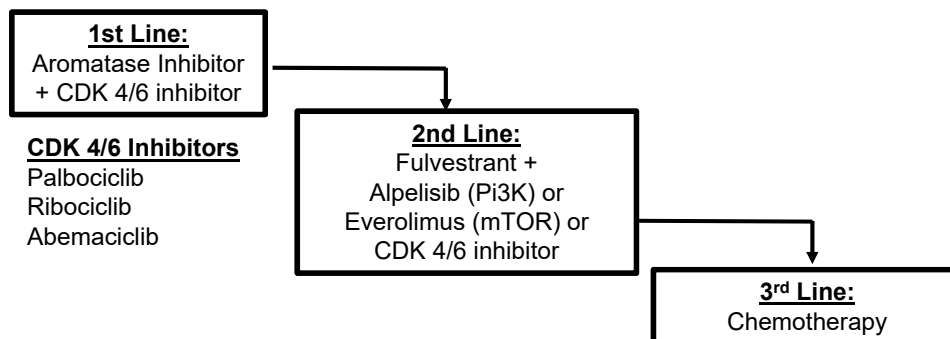


- Receptors determine if a patient will receive oral or IV chemotherapy for advanced disease
- There is a very limited role for surgery in metastatic breast cancer
- Radiation can help with pain associated with metastatic tumors

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Metastatic ER+/PR+ Breast Cancer

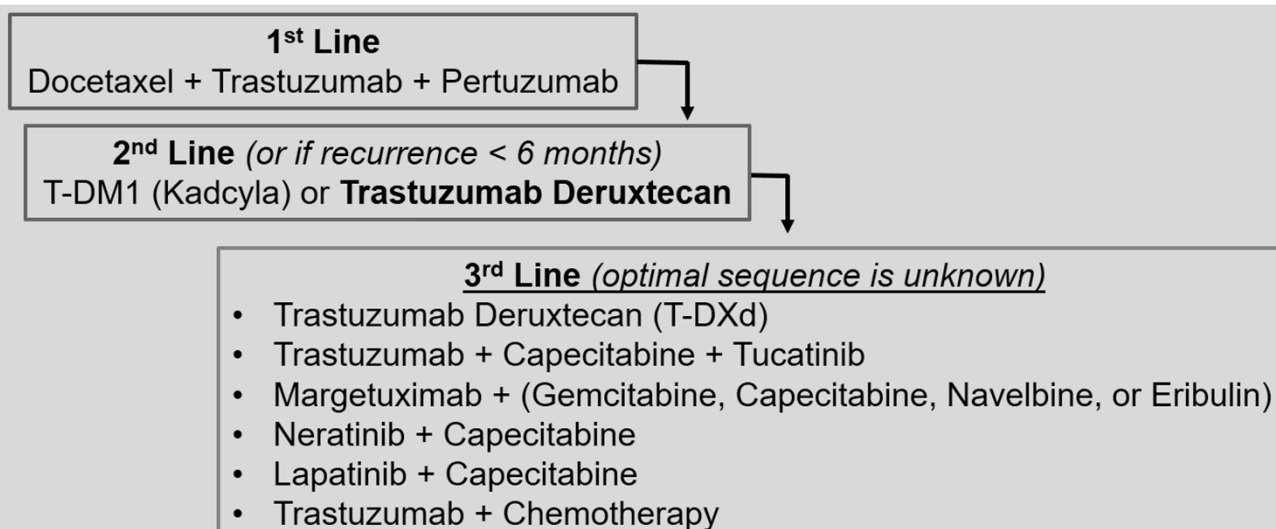
- First and second line treatment is generally oral chemotherapy



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Metastatic HER2+ Treatment Algorithm

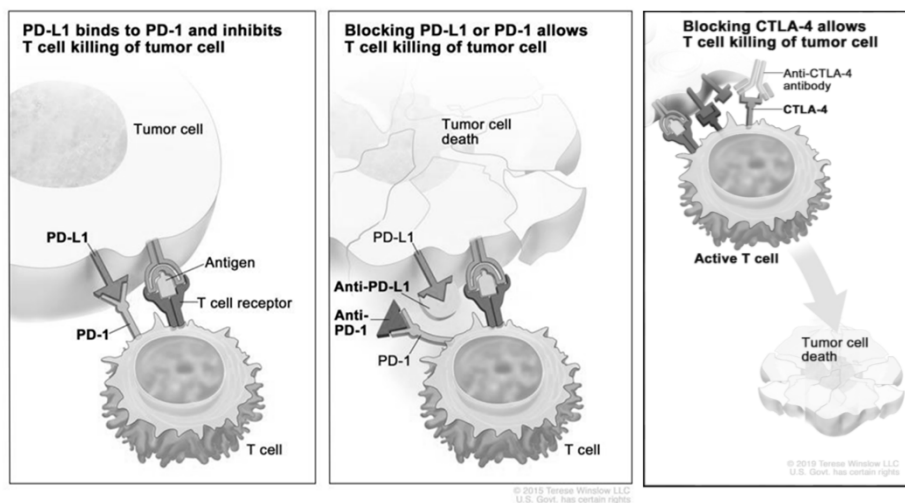
- Chemotherapy + HER2-Directed Antibody



Immunotherapy

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Immune Checkpoint Inhibitors (ICIs)



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Accessed 4/24/18: <https://visualsonline.cancer.gov/details.cfm?imageid=10396>
 Accessed 10/10/21: <https://nci-media.cancer.gov/pdq/media/images/776560.jpg>

Approved Indications for ICIs in Solid Tumors

- Most indications are for advanced/metastatic cancer, but some* are in earlier settings
 - Indications are for ICI +/- other agents (chemotherapy, small molecules, etc)

Lung Cancers

Non-Small Cell* ☐☐☐☐☐

Small Cell ☐☐

Pleural Mesothelioma ☐

Genitourinary Cancers

Kidney (Renal Cell) Cancer ☐☐☐☐

Bladder Cancer* ☐☐

Skin Cancers

Melanoma* ☐☐☐☐

Merkel Cell Carcinoma ☐☐

Squamous Cell Carcinoma ☐☐

Basal Cell Carcinoma ☐

Women's Cancers

Cervical Carcinoma ☐

Triple Negative Breast Cancer* ☐☒

Endometrial Cancer ☐☐

Gastrointestinal Cancers

Colorectal Cancer, MSI-H ☐☐☐

Hepatocellular Carcinoma ☐☐

Gastric/GE Junction/Esophageal ☐☐☐☐

Head and Neck, Squamous ☐☐

Not Tumor Specific

MSI-High ☐☐☐

TMB-High ☐

<input type="checkbox"/>	Nivolumab (Opdivo)	PD-1
<input type="checkbox"/>	Pembrolizumab (Keytruda)	
<input type="checkbox"/>	Cemiplimab (Libtayo)	
<input type="checkbox"/>	Dostarlimab (Jemperli)	
<input type="checkbox"/>	Atezolizumab (Tecentriq)	PD-L1
<input type="checkbox"/>	Durvalumab (Imfinzi)	
<input type="checkbox"/>	Aveumab (Bavencio)	
<input type="checkbox"/>	Ipilimumab (Yervoy) + nivolumab	

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<https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm>. Accessed Sept 29, 2021

Survival and ICI

- Patient outcomes are improved with ICI when compared to chemotherapy
 - Among responders, we see longer periods of disease control and better overall survival
- Ipilimumab (Nov 2011 FDA approved for metastatic melanoma)
 - Overall Cancer Death Rate significantly decreased in future years
 - Cancer Statistics 2020: ↓ by 29% from 1991 to 2017, with a **2.2% decline from 2016 to 2017**
 - Progress in treatment for melanoma drove the **most rapid death rate decline** seen, as the overall melanoma death rate dropped by 7% per year during 2013-2017.
 - Cancer Statistics 2021: ↓ by 31% from 1991 to 2018, with a **2.4% decline from 2017 to 2018**

Siegel et al. Ca Cancer J Clin. 2020. Siegel et al. Can Cancer J Clin. 2021.
 Sun et al. Scientific Reports. 2020.
 Accessed 10/13/20: <https://www.cancerresearch.org/immunotherapy/timeline-of-progress>

Approved FDA Indications of ICLs in Breast Cancer

Not Breast Cancer Specific

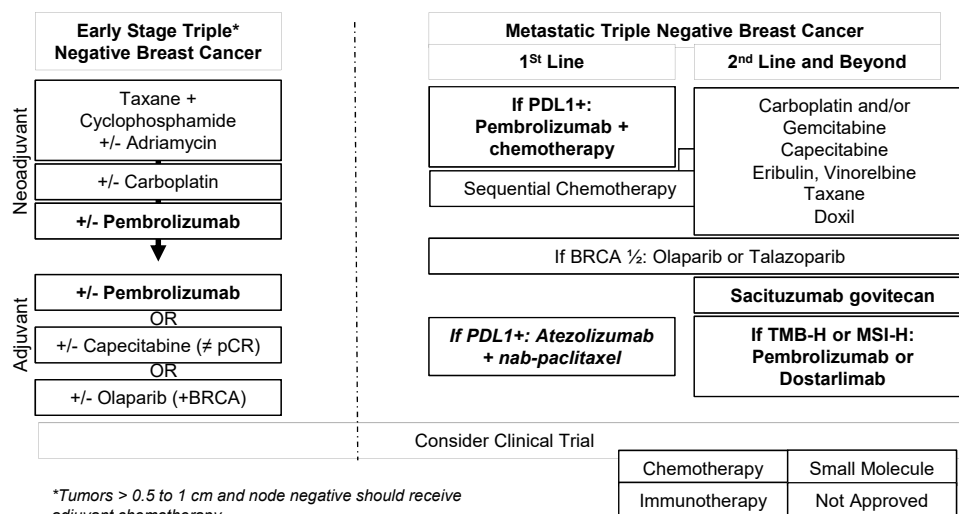
- **Pembrolizumab*** in MSI-High or mismatch repair deficient tumors
- **Pembrolizumab*** in TMB-High (≥ 10 mutations/megabase)
- **Dostarlimab*** in mismatch repair deficient tumors

Breast Cancer Specific

- ~~**Atezolizumab*** + Nab-Paclitaxel in 1st line, metastatic TNBC~~
- **Pembrolizumab** + Chemotherapy (nab-paclitaxel, paclitaxel or gemcitabine/carboplatin) in 1st line, metastatic TNBC
- **Pembrolizumab*** + neoadjuvant chemotherapy in early stage, high risk TNBC

*Accelerated approvals based on PFS, response rate/durability. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Triple Negative Breast Cancer Treatment



Learning Objectives

- ✓To Review Breast Cancer Basics
 - ✓Stats and Subtypes
 - ✓Sequencing of Local and Systemic Therapies
- ✓To Review Systemic Therapy of Breast Cancer
 - ✓Neoadjuvant Breast Cancer Treatment
 - ✓Adjuvant Breast Cancer Treatment
 - ✓Metastatic Breast Cancer Treatment for ER+ and HER2+
- ✓To Review Approved Indications for Immunotherapy in Breast Cancer
 - ✓Early and Adjuvant Triple Negative Breast Cancer