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# Quick Review: Breast Cancer

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## Abstract

Carcinoma of the breast affects 1 in 8 to one in 12 women over their life-time. The main risk factors are female sex, increasing age, and a genetic predisposition. In 1999, 176,000 women were diagnosed with breast cancer. The incidence of breast cancer is estimated at 86/100,000 women.

## ANATOMY

The breast is centered over the pectoralis major muscle. Its borders are the clavicle; sternum, 6th and 7th rib inferiorly, and is laterally bounded by the pectoralis and serratus anterior muscles. The innervation of the breast is derived from the anterior branches of the intercostal nerves 2 through 6 with the nipple receiving its innervation from the 4th intercostal nerve. The major blood supply in order of importance is the internal mammary branches, lateral thoracic, thoracodorsal perforating vessels from the pectoral branch of the throacoacromial branch of the axillary artery and small intercostals branches. Venous and lymphatic drainage parallel the blood supply. The breast tissue is composed of epidermis, dermis, superficial fascia, glandular breast tissue, deep fascial layer and the pectoralis major fascia and muscle. The glandular tissue consists mainly of epithelium, fibrous stroma, and fat. The breast is organized into roughly 20 lobular units made up of terminal ductals surrounded by fat and fibrous tissues and efferent ductules. These terminal ductals coalesce and drain towards the areola forming a single large duct that contributes to the nipple.

Breast cancer most commonly arises in ductal epithelium. DCIS or ductal carcinoma in-situ, and infiltrating ductal carcinoma are the most common types of cancer noted. Infiltrating ductal carcinoma accounts for up to 80% of all breast cancers.

It is hypothesized that DCIS is a precursor lesion to invasive cancer and is treated as such.

DCIS accounts for 15-25% of all breast cancers identified.

Lobular carcinoma in-situ (LCIS) is a benign condition and

is not associated with a mass.

LCIS is a predisposing marker of ductal carcinoma.

Infiltrating lobular carcinoma (LC) accounts for up 15% of all cases of breast cancer. It arises from the lobular unit of the breast and microscopically appears as small round cells; it is treated the same as invasive ductal carcinoma. LC may have a higher incidence of bilateral disease.

## INCIDENCE

Carcinoma of the breast affects 1 in 8 to one in 12 women over their life-time.

### Main

Increasing age

Genetic predisposition remain the.

- In 1999, 176,000 women were diagnosed with breast cancer.
- The incidence of breast cancer is estimated at 86/100,000 women.
- While the incidence is high, only 3.6% of American women will die from breast cancer.

There is much debate as to the utility of the screening mammography at this time. Women that are screened with mammography have an 80% overall chance of surviving the occurrence of breast cancer.

Prophylactic mastectomy may reduce the incidence by 90% in high risk women.

**GENETIC PREDISPOSITION HAS BEEN WELL DOCUMENTED**

Genetic factors are estimated to be involved in up to 5% of all breast cancers.

In patients younger than 30, this may play a more dominant role: up to 25% of breast

Cancers have a recognized genetic component.

BRCA 1 was initially discovered in 1994 on chromosome 17. It is an autosomal dominant gene involved in tumor suppression. It is estimated to be involved in 40 % of all familial breast cancers.

BRCA 2 was subsequently discovered on chromosome 13. It is estimated to account for up to 30% of the familial breast cancers. While BRCA 1 families have a genetic predisposition to ovarian cancer, BRCA 2 families appear to be spared.

**MECHANISMS OF SPREAD:**

- Direct Extension
- Regional Node Metastasis
- Hematogenous Metastasis

**TREATMENT:**

- Option A: Wide local excision, axillary dissection and radiation therapy
- Option B: Modified Radical Resection

Once a suspicious lesion is identified by mammography or examination, a complete history and physical examination is completed assessing the patient for risk factors of breast cancer.

A biopsy is obtained of the lesion. Options include fine needle aspiration, core biopsy, needle localized incisional/excisional biopsy or stereo tactically guided core biopsy. Stereo tactic core needle biopsy for non-palpable lesions may be the preferable method as it may avoid an operating room visit and gives stromal architecture unlike the FNA. Palpable lesions may also be biopsied with a core needle in clinic.

Ultrasound may be utilized to facilitate the initial biopsy.

Once a breast cancer is identified, standard local options

include lumpectomy/wide local excision [WLE] or mastectomy [MRM]. WLE removes the tumor and 1 to 2 cm of tissue surrounding the tumor. WLE and axillary dissection followed by postoperative radiation therapy (4500 cGy) has been shown to have equivalent survival rates to the modified radical mastectomy. MRM removes all the breast tissue anterior to the pectoralis muscle and includes an axillary dissection. There is currently some controversy regarding axillary dissection. Most surgeons are currently sampling the axilla by removing nodes located in axillary zones I, II, and part of level III. In the past all three levels were extirpated with a higher morbidity especially with regard to lymph edema without a proven survival benefit.

The local recurrence rate for WLE and axillary dissection is 12% versus 5% for the MRM. Sentinel node biopsy is currently being practiced by more surgeons. A nuclear emitting tracer attached to a colloid is injected either in the periareola dermis or in the stroma surrounding the tumor. Lymphozurim dye is also injected just prior to the skin incision in the same area and the first node draining the area (sentinel node) is identified by the gamma probe and the blue dye. If the node is positive for cancer on permanent section the rest of the axilla is extirpated at another setting. If the node is negative for malignancy the axilla is followed clinically. Long term survival data are currently being accumulated. However a false negative rate of 3.1% has been documented.

Currently minimally invasive techniques such as radiofrequency and cryoablation are under investigation as alternatives to WLE. The trend in extirpation for breast cancer is towards minimally invasive techniques such as WLE and sentinel node biopsy.

DCIS or ductal carcinoma in situ is treated in much the same as invasive cancers except that axillary dissection is not needed as only 2% of patients will have invasive or node positive disease. Patients at higher risk include those with comedo necrosis and tumors greater than 5 cm.

Lobular carcinoma in-situ is a benign condition and is not associated with a mass. It is a predisposing marker of ductal carcinoma. It is often diagnosed on core biopsy of some suspicious calcifications discovered on mammography. Women with LCIS have a thirty percent lifetime risk of developing invasive breast cancer. 50% of these subsequent cancers are lobular. Women with LCIS are followed closely with regular SBE and physician examinations and routine mammography.

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Once the tumor is extirpated, it should be sent for clinical markers such as the status of estrogen and progesterone receptors, ploidy, HER/2neu, erbB-2, and MIB status.

Adjuvant chemotherapy is currently being offered to node negative as well as node positive patients at increased risk for recurrence. Patients at higher risk include those with positive lymph nodes, tumor size greater than 1 cm, poor nuclear grade, high proliferative fraction or more cells in S-phase, aneuploid, negative progesterone and estrogen receptors and a higher MIB fraction.

Adjuvant chemotherapy offers a 20-30% improvement in long term survival. A discussion with the oncologist and the patient is necessary before therapy is initiated in order to assess the possible benefits and the risks associated chemotherapy. Common regimens include CMF [cyclophosphamide, methotrexate and 5-fluorouracil], CAF [cyclophosphamide, doxorubicin, and fluorouracil] with a hormone receptor modifier such as tamoxifen or ovarian ablation. New therapies and regimens are the norm.

### COMMONLY UTILIZED CHEMOTHERAPY REGIMENS:

- CMF: Cyclophosphamide 100mg/m<sup>2</sup> PO days 1 through 14. Methotrexate 40mg/m<sup>2</sup> IV days 1 and 8 with 5-Fluorouracil 600mg/m<sup>2</sup> IV days 1 and 8.
- CAF: Cyclophosphamide 600mg/m<sup>2</sup> IV day one, Doxorubicin 60mg/m<sup>2</sup> IV day one. 5-Fluorouracil 600mg/m<sup>2</sup> IV days 1 and 8.
- AC: Doxorubicin 60mg/m<sup>2</sup> IV and Cyclophosphamide 600mg/m<sup>2</sup> IV day 1. Repeat every 2 days for a total of four cycles.
- Neoadjuvant therapy for larger tumors and inflammatory cancers has shown some success in shrinking tumors preoperatively allowing for WLE. Neoadjuvant therapy does not affect the overall survival rate.

### Radiation therapy (XRT)

- Radiation therapy (XRT) is used to “sterilize” the remaining breast. XRT destroys cells by fracturing their DNA sequence through free radical creation and release. Radiation effects are optimized in well-perfused tissues that are rapidly turning over.
- Radiation therapy was first utilized in 1924. Since

that time it has used to provide equivalent survival rates for women with appropriate features (larger breast size to tumor ratio, single tumors, negative surgical margins, no prior radiation, not pregnant) choosing wide local excision and radiation therapy compared with MRM.

- Complications associated with radiation therapy include fatigue, breast erythema and edema, ipsilateral extremity edema long term (5-17%), and rib fractures.
- Commonly utilized regimen:
  - 4500-5000cGy
  - 180-200cGy fractions for 5 days/wk (for a total of 5 weeks)

### KEY POINTS

1. Breast cancer affects one in eight women.
2. Patients will present with a palpable mass or positive mammography
  - a. Be sure to obtain both in order to assess both breasts
4. Most important risk factors include
  - a. Female
  - b. Age
  - c. Prior cancers
  - d. Positive family history
6. Other risk factors
  - a. Smoking
  - b. Nulliparity
  - c. No breast feeding
  - d. Fatty diets
  - e. Radiation exposure
8. “Tumors the rumor, tissues the issue”
  - a. Core needle biopsy
  - a. Palpable

- b. Ultrasound guided
  - c. Stereotactic
  - c. Needle localized biopsy
  - d. Incisional / Excisional biopsy
  - e. FNA
10. Local treatment options
- a. WLE with axillary dissection or sentinel node biopsy and radiation therapy
  - b. MRM
    - a. Involve a plastic surgeon
    - b. Consider reconstruction and contralateral mammoplasty
12. Systemic therapy
- a. Overall survival benefit of 20-30%
  - b. Is the benefit worth the morbidity
14. Prophylactic mastectomy
- a. Only a 90% reduction of risk for breast cancer
  - b. Offer to those at high risk
    - a. Positive history
    - b. BRCA1 or BRCA2
    - c. Positive family history

**TNM CLASSIFICATION OF BREAST CANCER**

**PRIMARY TUMOR (T)**

**REGIONAL LYMPH NODES (N)**

**DISTANT METASTASIS (M)**

**STAGE GROUPING**

**5 YR. SURVIVAL RATE/ STAGE**

**QUICK SCENARIOS:**

**1. INFLAMMATORY BREAST CA**

Biopsy lesion. Rule out metastases with Mammography bone scans and a CT scan of chest abdomen, brain and axilla. Consider utilizing neoadjuvant therapy with

FAC/CAFV/CMF if a response is obtained complete the mastectomy and axillary dissection followed by a course of radiation therapy and adjuvant chemotherapy. If no response is obtained with chemotherapy initially, then proceed with radiation therapy. Proceed with mastectomy if possible after radiation therapy and follow with adjuvant chemotherapy. Overall prognosis is poor with a median survival of 31 months

**2. DCIS ON BIOPSY REPORT**

Review prior mammography operative report and complete patient H&P. If core or needle localized open biopsy done to obtain the DCIS, proceed with local excision for clean margins or simple mastectomy. You want a clean centimeter margin if possible. If the lesion was less than 5 cm in diameter and without evidence of comedo necrosis, no axillary dissection is required (nodes positive < 2%). After WLE proceed with radiation therapy. Patient will require careful follow up of contralateral breast as well. Recurrence rates of 13% have been reported. Patients in whom their lesion was greater than 1.5 cm, with margins less than 1 cm and high grade may benefit from hormonal therapy. Sentinel node biopsy may be considered although its yield is low and it is unclear how to interpret the data at this time

**3. LCIS ON BIOPSY REPORT**

Regular mammograms and breast ultrasound.

**4. BREAST CA & PREGNANCY:**

Occurs in less than 1.5% of Breast cancers

Obtain a core biopsy. Proceed with excisional biopsy/WLE if possible under local anesthesia with fetal monitoring. Prior to proceeding obtain a neonatologist, anesthesiologist and obstetrical consultation. Treat patient as if she is not pregnant. Things to avoid during pregnancy include radiation therapy and chemotherapy. It is up to the patient and the physician teams to decide which risks are worth taking.

1st Term: Anesthesia is considered most risky to fetus during this trimester. If possible wait to second trimester then proceed with MRM. Consideration of WLE and XRT with adjuvant therapy only if therapeutic abortion is also considered 2nd Term: MRM 3rd Term: MRM. WLE with xrt after delivery is an option, but xrt cannot be give to lactating women.

**References**

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