Definitions Related to Breast Health and Breast Cancer

**Adenocarcinoma**—ca arising from lining of walls of many different organs

**Absolute risk reduction**-compares new treatment efficacy by subtracting incidence w/new treatment from the normally seen incidence

**Adjuvant treatment**-rx added to increase effectiveness of primary treatment. Examples are chemotherapy, hormonal therapy or radiation therapy following surgery.

**Aneuploid**-an abnormal cell defined by either fewer or more than normal number of chromosomes in a cell

**BRCA 1 and BRCA 2**-genes identified to increase risk of hereditary breast ca

**Breast conservation surgery**-surgery that removes cancer while saving the basic cosmetic appearance of the breast. May also include skin sparing/nipple sparing procedures.

**Calcifications**-small calcium deposits in breast tissue seen on mammograms. These are the results of cell death in both benign and malignant conditions.

**Carcinoma in situ**—early stage when ca confined to tissues of origin w/o spread outside area; highly curable ca.

**Comedo**—architectural pattern; noninvasive, in situ ca but more aggressive than cribiform & papillary

**Cribiform & papillary**-architectural pattern; noninvasive, in situ ca

**DIEP reconstruction**-reconstruction using blood vessels called Deep Inferior Epigastric Perforators w/ overlying skin and fat; muscle not used, reconnected to the breast defect.

**Doubling time**-time required for cell to double in number. Breast cancer doubles every 23-209 days \(\Rightarrow\) 1 cell doubling every 100 days = 1 cm growth in 8-10 yrs

**Ductal papillomas**-small noncancerous, finger-like growths in mammary ducts that may cause bloody nipple discharge. Commonly found in women 45-50 yo.

**Endocrine manipulation**-treating breast ca by changing hormone balance of the body to prevent hormone dependent ca cells from multiplying.

**Fat necrosis**-hard, noncancerous lump caused by destruction of fat cells in the breast due to trauma or injury.
Fibroadenoma—nocancerous solid tumor, most often seen in younger women.

Fibrocystic breast changes or condition—noncancerous breast condition w/ multiple cysts or lumpy areas in the breasts. May fluctuate with menstrual cycle, may be accompanied by discomfort or pain.

Flow cytometry—procedure performed by pathology demonstrating aggressiveness of tumor; how many cells are in the dividing stage at one time, reflecting how rapidly the tumor is growing.

Galactocle—clogged milk duct often associated with childbirth.

HER2/NEU—human epidermal growth factor receptor 2→protein identified indicating aggressiveness

Inflammatory carcinoma—very aggressive ca in the lymphatics of the breast; immediate rx w/ chemotherapy for disease control.

Klinefelter’s syndrome—chromosomal abnormality; extra x chromosome, lower testosterone w/ associated physical attributes & potential diminished fertility

Mammary duct ectasia—noncancerous breast disease usually seen in menopausal women. Duct in or beneath the nipple clog w/ cellular & fatty debris; may be accompanied by a gray to greenish discharge, palpable lump and inflammation causing pain.

Mastectomy
  - Modified radical mastectomy—breast, breast skin, nipple, areola & axillary lymph nodes removed, chest muscles are spared.
  - Radical mastectomy—breast, breast skin, nipple, areola, chest muscles & axillary lymph nodes removed.
  - Segmental mastectomy—portion of the breast removed including ca & surrounding margin of healthy breast tissue.
  - Subcutaneous mastectomy—removal of breast tissue but leaves outer skin, areola & nipple intact.

Needle localization—radiology procedure to mark area of suspicion in breast prior to surgery.

Neo-adjuvant chemotherapy—chemo given prior to surgery to treat breast ca.

Oncogene—stretch of DNA. Genes that when inappropriately activated, contribute to malignant transformation of the cell.

Oncotype DX—evaluating known genes in tumor cells of women w/ early stage breast ca to evaluate potential for breast ca recurrence & need for chemo
Relative risk reduction—blanket statement of occurrence with new rx compared to standard--% of how much less.

SERMS [selective estrogen receptor modulators] antihormonal drugs that slow down/stop growth of cancers that need estrogen to grow; tamoxifen, toremifene, and raloxifene


Risk Models

Claus—subpopulation w/ autosomal dominant genetic allele known to increase risk from 20-92% [forerunner of BRCA]

Gail—nonhereditary risk factors w/ limited family hx http://www.cancer.gov/bcrisktool
  • Project risk over 5 yrs and lifetime
  • Who should use chemoprevention

BRACAPRO http://bcb.dfcicancer.org/bayesmendel/brcapro.php
  Evaluate for need to test for BRCA genes and use of MRI in screening.

Tyler Cuzick http://www.ems-trials.org/riskevaluator
  Evaluation for a gene predisposing to breast cancer in addition to the BRCA genes. The woman's family history is used to calculate the likelihood of her carrying an adverse gene, which in turn affects her likelihood of developing breast cancer.


Guide to path report www.breastcancer.org

Comparative Effectiveness of Therapies for Reducing the Risk of Primary Breast Cancer: Guidance for Shared Decision Making http://ce.effectivehealthcare.ahrq.gov/credit/?code=CER10
### Mammographic Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 0</td>
<td>Abnormal but inconclusive, additional study/views needed</td>
</tr>
<tr>
<td>Category 1 &amp; 2</td>
<td>Normal, repeat 1-2 yr</td>
</tr>
</tbody>
</table>
| Category 3 | A. Close observation suggested  
B. Abn finding, explainable  
** known or highly suspicious of malignancy |
| Category 4 | Abnormal finding, bx suggested [subcategories may be listed] |
| Category 5 & 6 | Known or highly suspicious of malignancy |

### Breast infections and appropriate antibiotics

<table>
<thead>
<tr>
<th>Type of infection</th>
<th>Organism</th>
<th>PCN allergy</th>
<th>Potential β-lactamase resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal lactational, skin associated</td>
<td>Staph aureus</td>
<td>Erythromycin</td>
<td>Amoxicillin-clavulanate</td>
</tr>
<tr>
<td>Non-lactational hidradenitis suppurativa</td>
<td>S. Aureus Enterococcus Streptococcus Bacteroides</td>
<td>Combination of erythromycin &amp; metronidazole</td>
<td>Amoxicillin-clavulanate</td>
</tr>
</tbody>
</table>

*Harris, Diseases of the Breast, 2004*
Most breast cancers are hormone-receptor-positive.

**ER+**: About 80% of breast cancers are estrogen-receptor positive.

**ER+/PR+**: About 65% of estrogen-receptor-positive breast cancers are also progesterone-receptor-positive. This means that the cells have receptors for both hormones, which could be supporting the growth of the breast cancer.

**ER+/PR-**: About 13% of breast cancers are estrogen-receptor-positive and progesterone-receptor-negative. This means that estrogen, but not progesterone, may be supporting the growth and spread of the cancer cells.

**ER-/PR+**: About 2% of breast cancers are estrogen-receptor-negative and progesterone-receptor-positive. This means that the hormone progesterone is likely to support the growth of this cancer. Only a small number of breast cancers test negative for estrogen receptors but positive for progesterone receptors. More research is needed to better understand progesterone-receptor-positive breast cancers.

**ER-/PR-**: If the breast cancer cells do not have receptors for either hormone, the cancer is considered estrogen-receptor-negative and progesterone-receptor-negative (or “hormone-receptor-negative”). About 25% of breast cancers fit into this category.

Any positive test result — whether just for estrogen receptors, just for progesterone receptors, or both — means that the breast cancer is considered “hormone-receptor-positive.” Hormonal therapy may help to slow or stop the growth of hormone-receptor-positive breast cancers by lowering your body’s estrogen levels or blocking the effects of estrogen. These medications also may reduce the risk that the cancer will come back (recur).

If your cell sample tests positive, your doctor usually will prescribe some form of hormonal therapy at some point in your treatment plan. If the breast cancer is hormone receptor-negative (ER- and PR-), your doctor is unlikely to recommend hormonal therapy. But remember that many other effective treatments are available.
Hormonal Therapy for Breast Cancer

The main types of hormonal therapy that may be used include:

**Selective estrogen-receptor response modulators (SERMs).** SERMs block the effects of estrogen in the breast tissue by attaching to the estrogen receptors in breast cells. Tamoxifen is the SERM most commonly used to treat breast cancer. Another SERM called Fareston (chemical name: toremifene) is sometimes used to treat advanced breast cancer in postmenopausal women.

**Aromatase inhibitors.** Aromatase inhibitors stop the production of estrogen in postmenopausal women. Aromatase inhibitors work by blocking the enzyme aromatase, which turns the hormone androgen into small amounts of estrogen in the body. This means that less estrogen is available to stimulate the growth of hormone-receptor-positive breast cancer cells. Aromatase inhibitors can't stop the ovaries from making estrogen, so these medications only work in postmenopausal women. The main sources of the hormone for those women are the adrenal glands and fat tissue, not the ovaries. Aromatase inhibitors include Arimidex (chemical name: anastrozole), Aromasin (chemical name: exemestane), and Femara (chemical name: letrozole).

**Estrogen-receptor downregulators (ERDs).** Estrogen receptor downregulators, called ERDs for short, block the effects of estrogen in breast tissue. ERDs sit in the estrogen receptors in breast cells. If an ERD is in the estrogen receptor, there is no room for estrogen and it can't attach to the cell. ERDs also reduce the number of estrogen receptors and change the shape of breast cell estrogen receptors so they don't work as well. Faslodex (chemical name: fulvestrant) is an ERD that may be used to treat advanced, hormone-receptor-positive breast cancer in postmenopausal women if other hormonal therapy medicines, such as tamoxifen, are no longer working.

**Luteinizing hormone-releasing hormone agents (LHRHs).** LHRHs shut down the ovaries and stop them from producing estrogen, which means less estrogen is available to help support the growth of hormone-receptor-positive breast cancer. LHRHs are usually given by injection once a month for several months, or every few months. Premenopausal women with early-stage, hormone-receptor-positive breast cancer can be treated with LHRHs. Examples include Zoladex (chemical name: goserelin), Lupron (chemical name: leuprolide), and Trelstar (chemical name: Triptorelin). When the medicine is stopped, the ovaries begin functioning again. The time it takes for the ovaries to recover can vary from woman to woman.

Other hormonal therapies may be used to treat advanced breast cancer that is hormone-receptor-positive and does not respond to the treatments listed above. Megace (chemical name: megestrol) is a form of progestin that suppresses the effects of estrogen on breast cancer cells. Halotestin (chemical name: fluoxymesterone) is an anabolic steroid that lowers the amount of estrogen in the body.
Several strategies have been developed to treat hormone-sensitive breast cancer, including the following:

**Blocking ovarian function**: Because the **ovaries** are the main source of estrogen in **premenopausal** women, estrogen levels in these women can be reduced by eliminating or suppressing ovarian function. Blocking ovarian function is called **ovarian ablation**.

Ovarian ablation can be done surgically in an operation to remove the ovaries (called **oophorectomy**) or by treatment with radiation. This type of ovarian ablation is usually permanent.

Alternatively, ovarian function can be suppressed temporarily by treatment with drugs called **gonadotropin-releasing hormone** (GnRH) agonists, which are also known as **luteinizing hormone-releasing hormone** (LH-RH) agonists. These medicines interfere with signals from the pituitary gland that stimulate the ovaries to produce estrogen.

Examples of **ovarian suppression** drugs that have been approved by the U.S. Food and Drug Administration (FDA) are **goserelin** (Zoladex®) and **leuprolide** (Lupron®).

**Blocking estrogen production**: Drugs called **aromatase inhibitors** can be used to block the activity of an enzyme called aromatase, which the body uses to make estrogen in the ovaries and in other tissues. Aromatase inhibitors are used primarily in **postmenopausal** women because the ovaries in premenopausal women produce too much aromatase for the inhibitors to block effectively. However, these drugs can be used in premenopausal women if they are given together with a drug that suppresses ovarian function.

Examples of aromatase inhibitors approved by the FDA are **anastrozole** (Arimidex®) and **letrozole** (Femara®), both of which temporarily inactivate aromatase, and **exemestane** (Aromasin®), which permanently inactivates the enzyme.

**Blocking estrogen’s effects**: Several types of drugs interfere with estrogen’s ability to stimulate the growth of breast cancer cells:

**Selective estrogen receptor modulators (SERMs)** bind to **estrogen receptors**, preventing estrogen from binding. Examples of **SERMs** approved by the FDA are **tamoxifen** (Nolvadex®), **raloxifene** (Evista®), and **toremifene** (Fareston®). Tamoxifen has been used for more than 30 years to treat hormone receptor-positive breast cancer.

Because SERMs bind to estrogen receptors, they can potentially not only block estrogen activity (i.e., serve as estrogen antagonists) but also mimic estrogen effects (i.e., serve as estrogen agonists). Most SERMs behave as estrogen antagonists in some tissues and as estrogen agonists in other tissues. For example, tamoxifen blocks the effects of estrogen in breast tissue but acts like estrogen in the uterus and bone.
Other antiestrogen drugs, such as fulvestrant (Faslodex®), work in a somewhat different way to block estrogen’s effects. Like SERMs, fulvestrant attaches to the estrogen receptor and functions as an estrogen antagonist. However, unlike SERMs, fulvestrant has no estrogen agonist effects. It is a pure antiestrogen. In addition, when fulvestrant binds to the estrogen receptor, the receptor is targeted for destruction.

**Characteristics of Hereditary, Familial and Sporadic Cancer Syndromes August 1, 2007**

In a recently published recommendations for risk assessment and genetic counseling for hereditary breast and ovarian cancer (HBOC) in a Journal of Genetic Counseling, there is a very useful definition of 3 main type of cancer (from a geneticist point of view):

I. “Hereditary Cancer type” characteristics:

- Apparently autosomal dominant transmission of specific cancer type(s)
- Earlier age of onset of cancers than is typical
- Multiple primary cancers in an individual
- Clustering of rare cancers
- Bilateral or multifocal cancers
- First degree relatives of mutation carriers are at 50% risk to have the same mutation
- Incomplete penetrance and variable expressivity, such that obligate carriers of the family mutation may be cancer-free and the age of diagnosis of cancer among relatives will vary
- Those who do not have the familial mutation have the general population risk for cancer

II. “Familial Cancer type” characteristics:

- More cases of a specific type(s) of cancer within a family than statistically expected, but no specific pattern of inheritance
- Age of onset variable
- May result from chance clustering of sporadic cases
- May result from common genetic background, similar environment and/or lifestyle factors
- Does not usually exhibit classical features of hereditary cancer syndromes

III. “Sporadic Cancers type” characteristics:

- Cancers in the family are likely due to nonhereditary causes
- Typical age of onset
- Even if there is more than one case in the family, there is no particular pattern of inheritance
• Very low likelihood that genetic susceptibility testing will reveal a mutation; testing *with available technology/knowledge level* will likely not provide additional information about cancer risk.

This classification can help in quantifying risks to individual family members and developing a plan for cancer screening, prevention, risk reduction and psychosocial support and counseling. It also helps in the determination of whether genetic testing is appropriate for the family, and if so, which relative(s) would be the appropriate individual(s) to test. Unfortunately, the separation of families into hereditary, familial, and sporadic cancer is often not precise.