Disease Information

Most breast tumors arise from duct epithelium, with the most common type being infiltrating ductal carcinoma that is not otherwise specified (NOS), accounting for 70% of breast cancer. Other histologic types of adenocarcinoma of the breast include medullary, lobular, mucinous, tubular, and papillary. Sarcoma, adenocystic, apocrine and squamous cell carcinoma of the breast are rarely seen and are generally ineligible for SWOG breast protocols.

Extent of nodal involvement is the most important prognostic factor for the development of metastatic disease. Approximately 55% of breast cancers are found before axillary node metastases have occurred. Women who have positive nodes (nodes containing cancerous cells) have a poorer prognosis than women whose nodes are negative or free of cancerous cells. The more nodes that are positive, the less favorable is the prognosis. Another important factor is hormone receptor status. Disease that is negative for estrogen and progesterone receptors tends to be more aggressive than receptor-positive disease. Recent investigations have suggested other factors, which may be important in identifying a patient at high risk for recurrence, such as HER2 status or high proliferation factors. The search for prognostic factors is particularly important in node negative disease, where the majority of patients enjoy extended survival without intensive treatment.

More than half of node positive patients recur within 10 years of diagnosis despite treatment. The most common distant metastatic sites for breast cancer are bone, lung, and liver.

Anatomy of the Breast

The breast is a glandular organ that produces milk (see Figure 1). It contains 15 to 20 lobes arranged like spokes around a wheel, and each lobe branches into lobules. Each lobule ends in 100 or so tiny bulbs called acini, where milk is produced. The spaces around and between the lobes are filled with fat. The lobes, lobules, and acini are connected to the nipple by a network of ducts, which enlarge as they enter the nipple. These enlargements are called the lactiferous sinuses.

The entire gland that is the breast - ducts, lobes, lobules, and acini - along with its supply of nerves, blood vessels and support structures is enclosed by a membrane called the fascia. The superficial fascia lies between the breast tissue and the skin; the deep fascia separates the breast tissue from the muscles of the chest wall.
Two muscles lie beneath the breast: the pectoralis major and the pectoralis minor. These muscles cover the ribs and aid in controlling arm movements. The breast tissue itself is held in position by the Cooper's ligaments, fibrous connections that run from the fascia, up between the lobes, to the skin.

Figure 1
Lymphatic System

The lymphatic system is a network of vessels and nodes that, together with tissues of the spleen, thymus, and bone marrow, constitutes the body's immune defense system.

Breast tissue is drained by lymphatic vessels lying in the spaces between and around the milk producing lobes. These vessels lead primarily to one of two clusters of lymph nodes: the axillary nodes, which lie in the armpit, and the internal mammary nodes, which lie along the sternum.

Lymph nodes in the axilla are frequent sites of breast cancer metastases. Malignant involvement may cause lymph nodes to become enlarged, hard and fixed to surrounding structures.

Treatment

There are four types of treatment generally used for breast cancer. Which one, or combination, that the physician chooses depends upon the stage of the disease, hormone receptor status, HER2 status, menopausal status and prior treatment.

Primary Surgery

Most patients who present with breast cancer have a surgical procedure to remove part or all of their breast(s), provided there is not yet detectable distant metastatic spread. The different surgeries are listed below.

Radical Mastectomy: Removal of the entire breast, skin, pectoralis major and minor muscles, and axillary lymph nodes. This is no longer recommended in most cases, as there is considerable morbidity and no evidence of superiority compared to lesser surgeries.

Modified Radical Mastectomy: Removal of axillary lymph nodes and the entire breast. The pectoralis minor muscle may also be removed.

Total (or Simple) Mastectomy: Removal of entire breast.

Breast Conserving Surgery: Radiation therapy is also generally given with any of these procedures:

Excisional Biopsy: Removal of the tumor. Previously was done to establish a diagnosis. Now, most patients with breast cancer are diagnosed by minimally invasive stereotactic or ultrasound-guided biopsy.

Lumpectomy/Partial Mastectomy: Removal of the tumor and small margin of surrounding tissue (the terms are often used interchangeably)
Quadrantectomy: Removal of the quarter of the breast that contains the tumor. This is generally not performed as often as it used to be. This procedure results in significant deformity of the breast, and if a large volume of tissue needs to be removed, the cosmetic results are often better with mastectomy and immediate reconstruction.

Axillary Dissection: Removal of some or all of axillary nodes. Currently a “lower level” or “Level I-II” dissection is performed. Surgical approach may be through the mastectomy incision or through a separate incision. Performance of a mastectomy with lymph node removal is considered a modified radical mastectomy. An axillary dissection can also be performed with breast conserving surgery.

Sentinel Node Biopsy: The sentinel lymph node is the first lymph node in a nodal basin to drain the primary tumor. It is identified using blue dye and / or radioactive technicium sulfur colloid injected into the breast tissue. The injection may be performed into the tissue immediately surrounding the primary tumor, into the skin, or into the subareolar region. If the sentinel node is negative for metastatic disease, axillary dissection can be avoided. Any node found to be blue, “hot”, and / or palpable is considered to be a sentinel node. Sentinel node biopsy is done through a much smaller incision than an axillary node dissection, and a drain is not left in place. There is still a small possibility for development of arm numbness and lymphedema.

Radiation Therapy
Radiation is given either by machine or implants. Radiation therapy is usually given when breast conserving surgery is performed, or if a mastectomy is performed but the patient presents with locally advanced disease (T3 – T4 lesion, positive axillary nodes). As part of initial treatment, it has been successful in helping to prevent local recurrence. In advanced disease, it may alleviate pain caused by bone metastasis.

More often, partial breast irradiation is performed in conjunction with breast conserving surgery. This allows radiation therapy to be given primarily to the tumor bed which is the site at most risk for recurrence of disease. Partial breast irradiation can be given using multiple catheters or newer balloon devices.

Systemic Therapy
Systemic therapies, e.g., additive hormone therapy, chemotherapy, biologic therapy, etc., may be used in both the adjuvant and advanced disease settings. Adjuvant therapy is administered after regional therapy (surgery and/or radiation) has rendered the patient disease free clinically, with the aim of eliminating microscopic disease. Most patients with axillary node involvement receive adjuvant therapy. Adjuvant therapy is becoming increasingly common in node negative disease as evidence accumulates demonstrating effectiveness in high risk subsets of these patients. Oncotype Dx and other genetic tests performed on the primary tumor may help to identify which node-negative patients may benefit from adjuvant chemotherapy. Patients who are diagnosed with advanced disease or disease that fails to be controlled by initial treatment are also treated with systemic therapy.
In cases of advanced disease at initial presentation, neoadjuvant chemotherapy and/or hormonal therapy may be given prior to surgery. There is no survival disadvantage if chemotherapy is given before or after surgery.

Additive Hormone Therapy: Systemic agents, e.g., estrogens or antiestrogens, are used to change hormone balance. This type of treatment appears to be most effective for patients whose tumors are estrogen receptor (ER) or progesterone receptor (PgR) positive. Hormones are used in adjuvant regimens, particularly for postmenopausal, ER positive, node positive patients. They are also the therapy of choice for advanced disease in ER positive patients, provided there is no life-threatening visceral involvement, such as lymphangitic lung metastases, brain metastases or liver metastases involving greater than one-third of the liver parenchyma. Two main classes of hormonal therapy are estrogen receptor blockers (tamoxifen) and aromatase inhibitors (anastrozole, letrozole, exemestane). Aromatase inhibitors are more effective than tamoxifen in post-menopausal women, but may accelerate osteoporosis.

Chemotherapy: Used both in adjuvant therapy regimens and for advanced disease with somewhat larger benefit in premenopausal patients.

Biological Therapy: Any form of treatment that uses the body’s natural abilities that constitute the immune system to fight disease. Recent developments in breast cancer include Herceptin for HER2+ disease.

Ablative Hormone Therapy
Ablative hormone therapy involves surgery (oophorectomy, adrenalectomy, hypophysectomy), used with the same rational as additive therapy. Oophorectomy is used primarily in premenopausal women. Use of adrenalectomy and hypophysectomy is now rare.