

Breast Cancer

Risk:

According to Box & Russell, 2004 breast cancer is the most common cancer in women and accounts for 29% of all cancers diagnosed each year. It is the overall second leading cause of cancer death, but the first in women under the age of 55.

Genetic Link:

The vast majority of breast cancers are diagnosed in women with no hereditary risk factors. Although 10-20 % of patients with breast cancer have a family history suggestive of a hereditary susceptibility only 5% of all breast cancers can be attributed to a known genetic defect (Box & Russell, 2004). The most common genetic defects are associated with **BRCA-1** and **BRCA-2**.

Indications for BRCA-1 and BRCA-2 Testing: (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005).

- Multiple cases of early onset breast cancer in a women's family history
- Breast and ovarian cancer in the same women
- Bilateral breast cancer
- Male breast cancer or
- Ashkenazi Jewish decent with breast cancer

For a summary about BRCA-1 & BRCA- 2 genetic testing click the following link

<http://www.geneclinics.org/profiles/brca1/details.html>

Hormones:

Exposure to estrogen and progesterone have been suggested to account for the majority of breast cancer risk as well as other risk factors such as early menarche, late menopause, delayed childbirth, and postmenopausal obesity (Box & Russell, 2004). According to Box & Russell, 2004 the Heart and Estrogen-progestin Replacement Study (HERS) and the Women's Health Initiative (WHI) trial have both demonstrated that hormone replacement therapy in postmenopausal women is associated with an increased risk of breast cancer. The studies suggested that if women used estrogen for longer than 5 years their risk of developing breast cancer increased by 35%. The addition of progesterone to estrogen increased this risk even further.

World Health Initiative advisory for the use of estrogen replacement therapy.
Click on the link below to review.

http://www.nhlbi.nih.gov/whi/e-a_advisory.htm

Other facts about the etiology of breast cancer include (Wood, Muss, Solin, & Olopade, 2005; Box & Russell, 2004; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Abraham & Zujewski, 2001; Franker, 2003)

- Age (incidence increases with age and steadily after age 50)
- Most forms of benign breast disease do not increase the risk of breast cancer
- Parity and lactation: women who completed their first full-term pregnancy after the age of 30 are 2-5 times more likely to develop breast cancer. The data on lactation are mixed but appear to indicate a decreased risk if women nurse for a long duration
- Physical activity reduces the risk regardless of what age the women is at
- Radiation exposure (ionizing radiation) increases the risk of breast cancer. Radiation to the chest (mantle field XRT for the treatment of Hodgkin lymphoma) can increase the risk by 30%
- Alcohol: there is a positive relationship between alcohol intake and increased breast cancer risk

Histology:

Poorly differentiated tumors (high grade) have a worse prognosis compared to well-differentiated (low grade). Inflammatory carcinoma has a poor prognosis, irrespective of stage (Wood, Muss, Solin, & Olopade, 2005; Box & Russell, 2004; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Abraham & Zujewski, 2001; Franker, 2003).

Histologic Types: (Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007).

- Ductal adenocarcinoma (70-80%)
- Lobular carcinoma (10%)
- Special types with a good prognosis (<10%) pure papillary, tubular mucinous, and typical medullary carcinomas
- Inflammatory carcinoma (1%) has the poorest prognosis
- Paget's disease of the breast: unilateral eczema appearance of the nipple
(always associated with DCIS in women)

To review an image depicting an inflammatory breast cancer click on the following link;

http://www.riverside-online.com/source/images/image_popup/br7_inflammatory.jpg

The following image is of a mammogram identifying an inflammatory breast cancer.

http://www.bodyofwealth.com/images/ibc_3.jpg

[A Word About Non-Invasive Cancer:](#)

[Ductal Carcinoma in Situ: \(DCIS\)](#)

Before screening mammography, the detection of DCIS was rare (3%). Today DCIS accounts for 10-20% of all diagnosed breast cancers. Also called intraductal carcinoma, DCIS is considered a preinvasive lesion but if it is left untreated, it will eventually progress to an invasive ductal carcinoma (Box & Russell, 2004). DCIS commonly presents itself on mammogram as areas of calcifications. As cancer cells are forming in the ducts they leave behind calcifications that are than noted on mammogram (Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Box & Russell, 2004). Patients will often require radiation therapy with or without hormone therapy (ex. Tamoxifen, Aromitase Inhibitors).

[Lobular Carcinoma in Situ : \(LCIS\)](#)

According to Box & Russell, 2004 the use of the term carcinoma in LCIS is misleading because LCIS is not considered a cancer. LCIS serves as a marker for subsequent development of invasive cancer. It does have the ability to convert to the invasive ductal form rather than the invasive lobular type. Women will have an increased risk of developing this invasive cancer for approximately two decades after diagnosis of LCIS. Patients with LCIS do not require radiation or chemotherapy. Patients are often safely followed with observation with or without hormone therapy.

Risk Assessment Models and tools are available and are often used by physicians to determine the chances of the patient developing an invasive breast cancer.

<http://www.cancer.gov/bcrisktool/about-tool.aspx>

A Word About Invasive Breast Cancers; (Ductal and Lobular)

Invasive Ductal Carcinoma:

Invasive ductal carcinoma is sometimes called infiltrating ductal carcinoma (Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Box & Russell, 2004). According to Box & Russell, 2004 this is the most common type of breast cancer accounting for approximately 75-80% of all cases. These cancers often arise from the duct system of the breast. They often present as stellate, irregular masses on mammography, or as a fixed, irregular mass on clinical exam. They are usually graded histologically (well differentiated, moderately differentiated, poorly differentiated). Poorly differentiated tumors are the most aggressive type. Keep in mind that a survival rate in an early stage cancer will drop steadily with an increasing tumor grade.

Invasive Lobular Carcinoma:

These types of tumors are also called infiltrating lobular carcinoma, arising from the lobular and terminal duct epithelium (Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Box & Russell, 2004). They account for 5-10% of all breast cancers (Box & Russell, 2004). Invasive lobular carcinoma is most often multicentric, involving multiple quadrants of the breast, and it can be bilateral. Radiation therapy is a challenge for these tumors because they rarely present themselves as stellate masses on mammogram. They will often appear as an area of architectural distortion without a mass. If a woman has dense breasts then this diagnosis may be difficult. This cancer tends to present as a diffuse infiltrative process that produces no clinically palpable or mammographically identifiable mass making early stage diagnosis difficult (Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Box & Russell, 2004).

Miscellaneous Breast Cancers: (inflammatory and Paget's Disease)

Inflammatory:

This type of breast cancer is rare and it tends to be aggressive. Inflammatory breast cancer accounts for 1-4% of all breast cancers (Box & Russell, 2004; Henke Yarbro, Hansen Frogge, & Goodman, 2005). This type of breast cancer is not known as a subtype. It is known as a clinical change that occurs as a result of breast cancer cells blocking the lymph channels in the breast (Box & Russell, 2004). The clinical presentation is typically evidenced by thick, erythematous skin (peau d'orange, similar to the skin of an orange).

Practitioners may confuse this type of cancer with mastitis. Unlike most of the breast cancers, therapy for this type of cancer usually begins with chemotherapy and rarely involves surgery (Henke Yarbro, Hansen Frogge, & Goodman, 2005).

Paget's Disease:

This disease is rare and does not tend to be invasive or life threatening. It appears as scaling, itching, or skin excoriation on or around the nipple and areola that does not heal with topical medication. It is almost never bilateral and may be confirmed by punch biopsy of the involved skin. Surgery is used to treat it (Box & Russell, 2004).

To Review the anatomy of the breast and axillary lymph nodes click on the following link

http://www.breastcancer.org/pictures/breast_anatomy/index.jsp

Location and Mode of Spread:

Most breast cancers are located in the upper outer quadrant. They spread by contiguity, lymphatic channels, and blood-borne metastases. The most common organs involved with metastases are regional lymph nodes, skin, bone, liver, lung, and brain (Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Box & Russell, 2004; Henke Yarbro, Hansen Frogge, & Goodman, 2005). Internal mammary nodes have evidence of tumor in 25% of patients with inner quadrant lesions and about 15% with outer quadrant lesions (Box & Russell, 2004). Internal mammary node metastasis is rare in the absence of axillary node involvement (Box & Russell, 2004).

Facts about the Clinical Course of the Disease: (Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Box & Russell, 2004; Henke Yarbro, Hansen Frogge, & Goodman, 2005)

- Trends based on stage
- Early breast cancer is curable
- Early breast cancer has a 10-20% chance of distant metastases occurring even in 10-20 years
- Locally advanced cancer has an increased risk of latent distant metastasis
- Metastatic breast cancer is not curable but usually has a course of stable disease on therapy and then progression in a stepwise fashion
- There are long-term survivors with metastatic breast cancer

Diagnosis:

Breast lumps are detectable in the majority of patients with breast cancer and constitute the most common sign on physical exam (Box & Russell, 2004). A typical breast cancer mass tends to be solitary, unilateral, solid, hard, irregular, and nontender. The second most common sign of breast cancer is spontaneous nipple discharge. It develops in 3% of women but 20% of men (Box & Russell, 2004; Henke Yarbro, Hansen Frogge, & Goodman, 2005). Breast cancer can be a manifestation of benign disease in 90% of patients. Discharge in patients older than 50 years of age is more likely to represent cancer (Box & Russell, 2004). Other presenting manifestations include skin changes, axillary lymphadenopathy, or signs of locally advanced or disseminated disease. A painful breast is common but usually the result of something other than cancer. Paget's carcinoma appears as a unilateral eczema of the nipple. Inflammatory carcinoma appears as skin erythema, edema, and underlying induration in the absence of infection (Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Box & Russell, 2004; Henke Yarbro, Hansen Frogge, & Goodman, 2005).

Evaluation of a Breast Lump:

If a woman is under 30 years of age, an ultrasound is the preferred diagnostic modality (Box & Russell, 2004). If the mass is solid and suspicious, then mammography followed by tissue diagnosis is recommended (Box & Russell, 2004). If the mass appears benign on mammogram then the options of tissue diagnosis versus observation with surveillance is appropriate. If the mass appears to be a complex cyst, then aspiration is appropriate. If the mass disappears with aspiration and the aspirate is bloody then routine screening can begin again (Box & Russell, 2004).

Breast lumps or masses in women over 30 years require a diagnostic mammogram. If the features are indeterminate, then ultrasonography should be performed. If the ultrasound shows a suspicious lesion, tissue sampling is required. Mammogram will detect approximately 85% of breast cancers (Box & Russell, 2004).

Patient's who have dense breasts, or a mass on exam with a normal mammogram and ultrasound, may undergo a breast MRI to further evaluate the mass (Wood, Muss, Solin, & Olopade, 2005).

The following web site provides additional information on imaging studies and the required preps for these studies

<http://www.imaginghealthcare.com/stereobreast.html>

A **breast biopsy** is required to make the final diagnosis of breast cancer. This may be done by;

- Fine-needle aspiration (FNA) cytology
- Ultrasound or stereotactic core biopsy
- Exisional biopsy

You will learn more about **staging and prognosis** in subsequent modules but here is a brief overview. Pre-staging work-up consists of;

- CBC, liver function tests
- CXR, diagnostic mammography
- Bone scan and radiologic evaluation of the liver if the patient is symptomatic or is found to have elevated alkaline phosphatase
- Bone marrow aspiration if unexplained cytopenia or a leukoerythroblastic blood smear

For an overview of breast cancer staging click on the following link;
<http://www.cancer.gov/cancertopics/wyntk/breast/page9>

Prognostic factors include tumor grade, pathologic stage (tumor size, lymph node involvement, distant metastasis, hormone receptor status, Her-2/neu overexpression) (Box & Russell, 2004). The higher the tumor grade the more guarded the prognosis. The **grade** is assessed by considering three features (tubule formation, nuclear pleomorphological, and count of mitoses) (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005).

The risk of **recurrence** increases with tumor size for patients with fewer than four lymph nodes involved with metastases. **Lymph node involvement** is the **greatest prognostic indicator** for breast cancer recurrence (Box & Russell, 2004).

Many patients with stage IV disease survive 2-4 years, depending on sites of metastases, their rate of progression, and response to therapy (Box & Russell, 2004).

Patients with tumors that are negative for both **ER** (estrogen receptor) and **PR** (progesterone receptor) have a slightly worse prognosis than those patients who have cancers with either ER or PR being positive (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005).

All cells, including breast cancer cells, carry two copies of the **HER-2/neu** gene (also known as the c-erb-2). Tumors that overexpress HER-2/neu tend to metastasize earlier and have a worse prognosis (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005). Tumors that express amplification of the HER-2/neu gene by fluorescent in situ hybridization (FISH) are those with the greatest potential to benefit from systemic monoclonal antibody therapy (**trastuzumab/Herceptin**) (Box & Russell, 2004).

Using **FISH amplification** > 2.0 is considered positive

Using **IHC** (score 0-3+) a score of 2+ or higher being positive

Management Options for Early Invasive Breast Cancer

Surgery:

Breast Conservation therapy: Total gross removal of tumor by limited surgery followed by XRT to eradicate residual tumor left in the remaining breast tissue (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005). Different names for this procedure are provided and are listed from most to least amount of tissue removed; quadrantectomy, segmentectomy, and lumpectomy (Box & Russell, 2004). An axillary node dissection or sentinel node procedure should be done for staging purposes with the surgery.

To review breast conservation therapy in detail click on the following link;

http://www.kcc.tju.edu/RadOnc/breast_therapy.htm

Modified Radical Mastectomy: Is the surgical procedure for patients who choose surgery as their only local treatment in an attempt to avoid radiation, or for those patients for whom breast conservation therapy is contraindicated (Box & Russell, 2004). This procedure includes complete removal of the breast as well as axillary lymph node resection (levels I and II (lower and middle) (Box & Russell, 2004).

To Review the procedure of a modified radical mastectomy click on the following link;

http://www.surgeryencyclopedia.com/images/gesu_02_img0154.jpg

Sentinel Lymph Nodes:

Nodal status is the single most important prognostic factor in breast cancer (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005). The number of lymph nodes involved has a major influence on decisions about adjuvant systemic treatment. Most physicians have replaced lymph node dissection with the blue node (use of isosulfan blue dye) or sentinel node technique, which allows a more limited removal of lymph nodes for staging purposes (Box & Russell, 2004). SLN theory is based on the concept that in breast cancer tumors smaller than 5 cm, the first lymph node in a lymph node bed to receive drainage from a tumor shows metastasis if there has been lymphatic tumor spread. When the SLN is tumor-free, there is a 98% accuracy that the tumor has not spread beyond the lymphatics (Box & Russell, 2004).

Currently the most accepted method is to use blue dye and a radiotracer. Most facilities will use both for increased accuracy of locating the SLN. Approximately 3 hours before the scheduled surgery, the patient is injected with a radiopharmaceutical. SLN procedure is usually done in the nuclear medicine suite of the radiology department. After the injection a dressing is put on and the site is massaged every 10-15 minutes for 90 minutes. After 90 minutes the patient is brought back to the nuclear medicine suite, where a series of anterior and lateral views produce a lymphoscintigraphy image. This image helps the surgeon in incision planning and assist in locating the SLN. The patient is taken to surgery and the isosulfan blue dye is injected around the tumor and the breast is massaged vigorously. After the patient is prepped and draped the surgeon excises the primary tumor. After the tumor is excised a hand-held gamma probe is used to assess the counts of radioactivity in the axillary area. "Hot" nodes are identified. The SLN is resected and sent for histological analysis. If micrometastatic disease is found than a follow-up axillary lymph node dissection (ALND) is necessary. If the SLN is negative than the patient's surgical therapy is complete. SLN procedures result in a lower rate of complications (lymphedema). It is generally unnecessary to use adjunctive XRT to the axilla after this procedure unless

there are four or more axillary lymph nodes involved by tumor or extensive lymphatic vascular invasion (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005).

To review the SLN procedure click on the following link;

<http://www.cancer.gov/cancertopics/factsheet/Therapy/sentinel-node-biopsy>

Breast Reconstruction:

Indications: include the availability of adequate skin and soft tissue for a reasonable cosmetic result and realistic patient expectations (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005).

Contraindications: inflammatory carcinoma, the presence of extensive radiation damage to the skin from prior treatment, unrealistic expectations on the part of the patient, and the presence of comorbid diseases that make surgery dangerous (Box & Russell, 2004).

Radiation Therapy: Used as an adjunct to breast conservation therapy in early stage disease, for patients with four or more axillary lymph node metastases, for local control of metastatic disease, and for locally advanced disease with positive margins (Box & Russell, 2004).

For women who undergo breast conservation, most of the radiation is given as external beam radiation to the entire breast (about 4,500 to 5,000 cGy) and the remainder is given as a boost to the area of the biopsy (1,000- 2,000 cGy). Newer products in clinical trials involve implanted devices that deliver radiation in the lumpectomy cavity in a shorter period of time and are then removed in lieu of giving whole-breast radiation (Box & Russell, 2004).

To review an image demonstrating external beam radiation therapy click on the following link;

<http://www.kcc.tju.edu/RadOnc/images/brstpic.jpg>

Adjuvant Chemotherapy:

Those who are considered for adjuvant chemotherapy include nearly all women with positive axillary lymph nodes and many with high-risk, node-negative disease (NCCN, Practice Guidelines, 2007; Box & Russell, 2004; Wood, Muss, Solin,

& Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Henke Yarbro, Hansen Frogge, & Goodman, 2005). Node-negative patients who are candidates for adjuvant chemotherapy are those with tumors that are hormone receptor negative, or moderately or poorly differentiated, or overexpress HER-2/neu. The benefit of chemotherapy is dependent on the women's age at diagnosis and her hormone receptor status (NCCN, Practice Guidelines, 2007; Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Henke Yarbro, Hansen Frogge, & Goodman, 2005).

Tumors that are hormone receptor negative have a greater relative reduction in risk of recurrence compared to women whose tumors are hormone receptor positive (Box & Russell, 2004). For women with early breast cancer but with poor prognostic markers, treatment recommendations must be made with a blend of the science and art of medicine (Box & Russell, 2004).

The National Comprehensive Cancer Network (NCCN) 2007 Breast Cancer Practice Guidelines recommend chemotherapy options for women based on their lymph node involvement:

http://www.nccn.org/professionals/physician_gls/default.asp

Lymph Node-Negative Breast Cancer	Lymph Node-Positive Breast Cancer
CMF (cyclophosphamide/ methotrexate/ 5-FU) FAC/CAF (cyclophosphamide/ doxorubicin/ 5-FU) AC (adriamycin/ cyclophosphamide)	CMF (cyclophosphamide/ methotrexate/ 5-FU) FAC/CAF (cyclophosphamide/ doxorubicin/ 5-FU) CEF (cyclophosphamide/epirubicin/ 5-FU) AC (adriamycin/ cyclophosphamide)

(Box & Russell, 2004)

Common Combination Chemotherapy Regimens for Breast Cancer

Regimen (cycle frequency)	Cyclophosphamide	5-Fluorouracil	Other
CMF (3 wk)	600	600	Mtx 40 (d 1)
Classic CMF (4 wk)	100 po (days 1-14)	600	Mtx 40 (d 1 and 8)
AC (3 wk)	600 (d 1)	-	Adr 60 (d 1)
FAC (4 wk)	400-500 (d 1)	400-500 (d 1 and 8)	Adr 40-50 (d 1)
CAF (4 wk)	100 po days (day 1-14)	600 (d1 and 8)	Adr 30 (d 1 and 8)

EC (3 wk)	600 (d 1)	-	Epi 100 (d 1)
CEF 120 (4 wk)	75 po (days 1 - 14)	500 (d 1 and 8)	Epi 60 (d 1 and 8)
FEC 100 (3 wk)	500 (d 1)	500 (d 1)	Epi 50 (d 1 and 8) Or 100 (d 1)
TAC (3 wk)	600 (d 1)	-	Adr 50 (d 1) Doc 75 (d 1)
Dose Dense AC (2 wk x 4) Then (2 wk x 4)	600 (d 1)	-	Adr 60 (d 1) Pac 175 (d 1)

Key: Adr = adriamycin

Doc = doxorubicin

Epi = Epirubicin

Mtx = methotrexate

Pac = paclitaxel

(Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007).

Special Note:

Women who over express HER-2neu will be candidates for Herceptin in the adjuvant setting. Historically, Herceptin was given when women were known to over express HER-2 neu in the metastatic setting. Because of the added risk of Herceptin with AC to cause cardiac complications, women may receive AC first followed by Herceptin in the adjuvant setting (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007). Follow-up echocardiogram or MUGA scans are recommended for women while receiving Herceptin therapy due to identified risks of a decreased ejection fraction with monotherapy.

To Review how Herceptin works click on the following link;

http://www.breastcancer.org/treatment/targeted_therapies/herceptin/how_it_works.jsp

Hormonal Therapy:

Tamoxifen has been considered the standard of care for pre menopausal women with an invasive breast cancer that expresses either ER or PR. The benefit of Tamoxifen is seen regardless of age, the number of involved lymph nodes, or whether or not chemotherapy is used. Tamoxifen is considered a selective estrogen receptor modifier (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007; Geddie, 2003; Abraham & Zujewski, 2001).

Aromatase inhibitors (AIs) block the peripheral conversion of the adrenal androgens (androstenedione and testosterone) into estradiol and estrone in women. AIs should not be considered in women who have any ovarian function as blockage of peripheral aromatization will block the ovarian production of estrogen and progesterone. Superiority of the AIs (Arimidex, Femara) over Tamoxifen in the metastatic setting in both disease free survival and time to progression has been observed (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007). In the adjuvant setting, post-menopausal women in with hormone receptor-positive invasive breast cancer now have the option of taking Tamoxifen or Arimidex. The addition of letrozole (Femara) may be added after 5 years of Tamoxifen. When chemotherapy and Tamoxifen are both used in the adjuvant setting, they should be used sequentially with all chemotherapy finished prior to initiating hormone therapy (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007).

To review the mechanism of action of Tamoxifen click on the following link;
<http://www.cancer.gov/cancertopics/factsheet/Therapy/tamoxifen>

To review the mechanism of action of Aromatase Inhibitors click on the following link;
http://en.wikipedia.org/wiki/Aromatase_inhibitor

Ovarian Ablation:

There is a similar benefit from surgical ablation of the ovaries as there is with the use of CMF chemotherapy in premenopausal women with ER + breast cancer (Box & Russell, 2004). Ovarian suppression with agonists of luteinizing hormone-releasing hormone (LHRH) likely gives the same benefit as surgical castration (Box & Russell, 2004). The following hormones can be used in a sequential manner:

Post-Menopausal Women	Pre-menopausal Women
Arimidex	Tamoxifen
Aromasin	LHRH agonist or surgical oophrectomy
Femara	Megestrol acetate
Nolvadex	Fluoxymesterone
Faslodex	Diethylstilbesterol
Megace	
Halotestin	
Diethylstilbestrol	

(Box & Russell, 2004).

Bisphosphonates are recommended for women with breast cancer metastatic to the bones (Box & Russell, 2004; Wood, Muss, Solin, & Olopade, 2005; Jardines, Hafty, Fisher, Weitzel & Royce, 2007). Both pamidronate (Aredia), zoledronate (Zometa), and ibadronate (Boniva) are effective in reducing bone pain and pathological fractures (Box & Russell, 2004). Zoledronate may be superior to pamidronate for reducing bony fractures, spinal cord compression, hypercalcemia of malignancy and for reducing the need for palliative XRT in patients with metastatic disease (Box & Russell, 2004).

For a comprehensive overview of the management of bone metastasis click on the following link;

http://www.cancer.org/docroot/CRI/content/CRI_2_4_4X_How_Is_Bone_Metastasis_Treated_66.asp

Special Considerations: (Henke Yarbrow, Hansen Frogge, & Goodman, 2005; Box & Russell, 2004)

- 6 months after completion of XRT those who have undergone breast-conserving therapy will have a repeat mammogram and then annually
- the goal of follow-up is to detect local-regional recurrent disease that is still amenable to curative therapy
- women should be seen at least annually after a diagnosis of breast cancer
- need to keep patients current with other screening modalities such as colonoscopy or cervical cancer screening
- post surgical edema may occur with less extensive surgery
- the incidence of post surgical edema is increased in patients who receive postoperative XRT
- edema usually develops within 6 months after surgery but may be delayed
- edema of the arm or paresthesias occurring more than 1 month after surgery may reflect recurrent tumor
- There is no relationship between breast implants and breast cancer
- Mammography techniques have been developed to assess the breast tissue in women with implants
- If a woman elects for mastectomy as part of local management and requires XRT to the chest wall placement of breast implants are usually avoided

Nursing Management: (Henke Yarbro, Hansen Frogge, & Goodman, 2005; Carpenter & Elam, 2003).

- Educate patient to continue monthly breast self exams (risk of recurrent disease or contralateral breast cancer)
- Instruct patient regarding the potential risks and benefits of **hormonal therapy** (efficacy, optimal dose, side effects)
- Educate and reinforce patient knowledge regarding **stage** of disease, treatment options and prognosis
- Educate patient regarding the **SLN procedure** for evaluating nodal disease (lymph node involvement on the affected side). Instruct patient that they will have a blue hue to their skin post procedure related to the injected color of the dye used during the procedure
- Educate patient that the risk of **lymph edema** may be lessened by SLN procedure (although not studied) due to the limited number of lymph nodes removed. Continue to encourage patients to practice good skin hygiene, avoid having blood drawn, injections, and infusions in the affected arm, wear protective clothing when working outside, do not cut hangnails or cut nails short, exercise the affected arm (full ROM and strength of the affected arm should return in a couple months

<http://www.com.msu.edu/pmr/lymphedema.htm>

- Patients can expect to resume all activities of daily living in a couple of months
- Reinforce key points about **radiation therapy**
 1. Radiation therapy is a local treatment that is intended to kill cancer cells
 2. **Daily treatments** (5 days a week for a determined period of time) are painless; skin and hair follicle cell lines demonstrate changes more rapidly because of higher mitotic activity. The effects generally resolve a few weeks after the completion of therapy
 3. Instruct patient to **avoid** sun, heating lamps, ice packs, harsh soaps, adhesive tape to area, do not shave or wear deodorant under the arm being treated. Patients are to avoid tight bras or underwire bras.
 4. Use only unscented hydrophilic creams (Aquaphor, Biafine), 99-100% pure aloe vera gel and Radiacare gel or gel pads
 5. Radiation treatments will often cause pain and discomfort over time due to skin erythema, dryness, tightness of the skin and/ or desquamation
 6. For **local irritation** (itching/folliculitis) diphenhydramine may be used
 7. The radiated breast may show signs of hyperpigmentation approximately 2 weeks after the start of treatment. Discoloration will lessen over time after the end of treatment. Mild hyperpigmentation may last for months

8. Occasional aches and pains in the treated breast/chest wall may continue for weeks or months after finishing RT. The use of analgesics may be required
9. **Breast tissue** may feel thicker and firmer after RT. Patients should be instructed to continue self-breast examinations monthly in order to remain familiar with the feel of the breast tissue
10. **Treatments last** approximately 15 mins- 30 mins including set up times. Set up time is longer than the actual treatment time
11. Radiation therapy decreases the chance of cancer recurring
 - Teach patient to report localized pain of gradually increasing intensity that does not go away (need to evaluate for skeletal metastases)
 - Teach patient to report signs of **progressive back pain** (localized and radicular), muscular weakness (lower extremities), paresthesias in one or more extremities, loss of bowel/bladder sphincter function
 - Assess and report patient complaints of **headache** (persistent, primarily in AM upon awakening), unilateral sensory loss, focal muscular weakness, hemiparesis, ataxia, visual defects, aphasia (speech disorders), impaired cognition, mental status changes, papilledema, persistent nausea/vomiting (9-25% of all patients with breast cancer will develop brain metastases. Twenty-five - 50% of all patients with metastatic breast cancer will develop brain metastases.)
 - Evaluate and report any **changes in respiratory status**; chest pain, dyspnea, nonproductive cough, rule out pleural effusion
 - Assess and report unresolved **GI complaints** (58-65% of all breast cancer patients will have at time of death)
 - Evaluate and document the impact of diagnosis and treatment on patients **QOL**
 - Discuss and educate patients regarding expected side effects related to the most commonly used agents for the **treatment** of breast cancer (alopecia, stomatitis, weight gain, fatigue, myalgias, arthralgias, thromboembolic events, nausea and vomiting, neutropenia)
 - Educate patients that **weight gain** incidence varies from 50-90% with a weight gain greater than 10% (up to 22 pounds) and duration up to two years after treatment. Note that other factors may contribute to this phenomenon; fatigue, depression, hormonal changes, and metabolic imbalances
 - Inquire about **hot flashes** and note increases or decreases in physiologic response with time

- Review **pharmacologic management** of hot flashes; venlafaxine, gabapentin, clonidine, bellergal, megesteral, vitamin E
- Review risks for **osteoporosis** related to aromatase inhibitors or early menopause (baseline DEXA scan should be ordered and annually thereafter while patient is on treatment). Discuss prevention strategies; exercise 30 minutes a day, 3 times a week, weight training, prevent falls, calcium 1200mg – 1500mg with vitamin D 1200 international units (this dose is a new guideline increase from 400), avoid taking calcium supplements with caffeine which may affect calcium, stop smoking and decrease alcohol intake.
- Consider and assess for **late effects** of both chemotherapy and radiation therapy; pulmonary toxicity, impaired cognitive functioning (“chemo brain”), neurosensory effects (neuropathies), secondary cancers, hemorrhagic cystitis, rib fractures, skin changes
- Assess for signs of anxiety and depression (survivorship, chronic illness, risk of recurrence, social challenges)
- Consider **end-of-life** symptom clusters; pain, delirium. Dyspnea, anorexia/cachexia, depression