All About Breast Cancer

What is the breast?

The breast is a collection of glands and fatty tissue that lies between the skin and the chest wall. The glands inside the breast produce milk after a woman has a baby. Each gland is also called a lobule, and many lobules make up a lobe. There are 15 to 20 lobes in each breast. The milk gets to the nipple from the glands by way of tubes called ducts. The glands and ducts get bigger when a breast is filled with milk, but the tissue that is most responsible for the size and shape of the breast is the fatty tissue. There are also blood vessels and lymph vessels in the breast. Lymph is a clear liquid waste product that gets drained out of the breast into lymph nodes. Lymph nodes are small, pea-sized pieces of tissue that filter and clean the lymph. Most lymph nodes that drain the breast are under the arm in what is called the axilla, or armpit.

What is breast cancer?

Collections of cells that are growing abnormally or without control are called tumors. Tumors that do not have the ability to spread throughout the body may be referred to as benign. They are not cancer. Tumors that have the ability to grow into other tissues or spread to distant parts of the body are referred to as malignant (cancerous). Malignant tumors within the breast are called breast cancer. Theoretically, any of the types of tissue in the breast can form a cancer, but cancer cells are most likely to develop from either the ducts or the glands. These tumors may be referred to as invasive ductal carcinoma (cancer cells developing from ducts) or invasive lobular carcinoma (cancer cells developing from lobes).

Sometimes, precancerous cells may be found within the breast tissue. These are referred to as ductal carcinoma in-situ (DCIS) or lobular carcinoma in-situ (LCIS). DCIS represents about 20% of all breast cancers. Because DCIS cells may become capable of invading breast tissue, treatment for DCIS is usually recommended. In contrast, LCIS is considered to be a marker for increased risk for breast cancer, but it does not usually need to be treated unless a true breast cancer is also present.

This article focuses on breast cancer in women. Click here information about male breast cancer.

What causes breast cancer and am I at risk?

Breast cancer is the second most common malignancy affecting women in America. Being a woman puts you at a higher risk of getting breast cancer. Women have more estrogen and progesterone (female hormones), which can promote breast cancer cell growth.

An estimated 268,600 cases of female breast cancer are diagnosed annually. Approximately 12.8% of women will develop breast cancer at some point in their lifetime. Men can develop breast cancer, but breast cancer is about 100 times more common in women.

As any woman ages, her risk of breast cancer increases. Risk is also affected by the age when a woman begins menstruating (younger age may increase risk), and her age at her first pregnancy (older age may increase risk). Taking estrogen, which can be in the form of hormone replacement therapy (HRT), may increase breast cancer risk.
Caucasian women are slightly more at risk of developing breast cancer than African-American women. However, women diagnosed under the age of 45, are more likely to be Africa-American women. Asian, Hispanic, and Native-American women have the lowest risk of being diagnosed with breast cancer.

**Dense Breast Tissue and Benign Lesions**

Dense breast tissue is also a risk factor for breast cancer. Dense breasts tend to be made up of more glandular and fibrous tissue than fatty tissue. Having dense breast tissue is common, found in about 40% of women. Breast tissue can change over the course of a woman’s life. Dense breasts can make it more difficult for a radiologist to read a mammogram. Studies have found that a 3D mammogram (also called tomosynthesis) or breast MRI may better detect abnormalities in women with dense breast tissue. There are a few benign breast conditions that are considered risk factors for developing breast cancer later. These include LCIS (mentioned above), atypical lobular carcinoma, atypical ductal hyperplasia, and atypical hyperplasia.

**Family History and Genetic Mutations**

Family history is very important in determining breast cancer risk. While you would think that a history of cancer in the family would automatically increase risk, it isn't so simple. Some common cancers – like breast and prostate – are seen in many families but do not necessarily increase risk in that family, particularly if the person was older at the time of diagnosis. Having an elderly grandmother diagnosed with breast cancer does not increase your risk much, but a mother diagnosed at 43 does. There is no one size fits all explanation, so it is important to discuss your family history and risk with your healthcare providers.

Known genetic mutations that increase the risk of breast cancer are present in some families; these include mutations in the genes **BRCA1** and **BRCA2**. Between 5% and 10% of breast cancers may be related to changes in one of the BRCA genes. Women can inherit these mutations from their parents, or mutations can arise for the first time in an individual. You should consider genetic testing if you or a family member has had:

- Breast cancer at age 50 or younger
- Triple-negative breast cancer at age 60 or younger
- Ovarian or fallopian tube cancer at any age
- More than one breast cancer diagnosis
- Male breast cancer
- Breast, ovarian, or pancreatic cancer and are of Ashkenazi Jewish ancestry
- A known mutation in a cancer risk gene
- Breast, ovarian, pancreatic, or high-grade prostate cancer diagnosed in multiple individuals on the same side of the family.

If a woman is found to carry either mutation, she has a much higher chance of developing breast and ovarian cancer. (Learn more about risk with BRCA1/2 mutations).

Family members may elect to be tested to see if they carry the mutation as well. If a woman does have the mutation, she may choose to undergo more rigorous screening or even undergo a preventive (prophylactic) mastectomy or oophorectomy to decrease her chances of developing breast or ovarian cancer. The decision to undergo genetic testing is a highly personal one that should be discussed with a genetic counselor who is specially trained to counsel patients regarding the risks and benefits of genetic testing.

**History of Radiation**

Another factor that puts a woman at higher risk of being diagnosed with breast cancer is a history of treatment with radiation to the chest. This risk is highest in women who received chest radiation during adolescence when the breasts were in development. If you received radiation to the chest wall, be sure your provider knows about this to make decisions about your screening needs. Some women will be advised to have a breast MRI in addition to a mammogram for screening.

**History of Breast Cancer**

If you have had breast cancer in the past, you are 3 to 4 times more likely to develop another breast cancer compared to a woman who has never had the disease. This is not metastases or spread from the first cancer, but a new cancer altogether.
This may occur in the same breast or the other breast. This is why it is so important to keep follow up appointments with your oncology team and continue recommended screening tests.

DES Exposure

DES was the first synthetic estrogen and was given to pregnant women from 1938-1971 because it was believed to prevent miscarriages and promote "healthy pregnancies." It was found that not only did the drug not prevent problems associated with pregnancy, it also caused health issues for the women taking it, as well as children born of these pregnancies. Women who took DES have been found to have a "moderately" increased risk of developing breast cancer. Studies have found a 30% increased risk compared to women who did not take DES. Women who were given DES should have annual mammograms and breast exams by a healthcare provider. They should be familiar with their normal breast tissue and report any nipple discharge or changes in their breast tissue or skin (dimpling, swelling, redness, nipple retraction) to their healthcare provider. Women who were given DES during pregnancy should be sure their children know this and report it to their healthcare team. Daughters born to women taking DES (DES daughters) are at increased risk of breast, vaginal and cervical cancers and should discuss screening recommendations with their healthcare providers.

Modifiable Risk Factors

Some factors associated with breast cancer risk can be controlled by a woman herself — called “modifiable” risk factors. Use of hormone replacement therapy (HRT), drinking more than 5 alcoholic drinks per week, being overweight, and being inactive may all contribute to breast cancer risk. It is important to remember that even someone without any risk factors can still get breast cancer. Proper screening and early detection are our best weapons in reducing the mortality associated with this disease.

How can I prevent breast cancer?

The most important risk factors for the development of breast cancer, such as age and family history, cannot be controlled. However, some risk factors may be in a woman's control. These include things like avoiding long-term hormone replacement therapy use, having children before the age of 30, breastfeeding, avoiding weight gain through exercise and proper diet, and limiting alcohol consumption to 1 drink a day or less.

Women at very high risk due to family history may benefit from chemoprevention, which means taking a medication or supplement to prevent the development of cancer. A category of medications called selective estrogen receptor modulators (SERMs) work by blocking the effect of estrogen on certain tissues in the body, including breast tissue. In doing so, they can reduce the risk of developing breast cancer by as much as 50% in women at high risk. The two most studied SERMs are tamoxifen and raloxifene. These medications do have their own risks, so whether or not to take them as chemoprevention is a discussion each woman should have with her healthcare provider.

What screening tests are available?

The earlier that breast cancer is detected, the more likely it is to be curable. Screening mammograms are simply x-rays of the breasts. Each breast is placed between two plates for a few seconds while the x-rays are taken. If something appears abnormal, or better views are needed, magnified views or specially angled pictures are taken. Mammograms often detect tumors before they can be felt and they can also identify tiny specks of calcium that could be an early sign of cancer. The majority of breast cancers are detected through abnormal mammogram findings.

Currently, there is much discussion as to when and how often a woman should have a mammogram. Current recommendations from the American Cancer Society state:

- Women ages 40-44 should have the choice to start screening mammograms after discussing the risks and benefits with their provider.
- Women aged 45-54 at average risk should have a screening mammogram annually.
- Women aged 55 and older should get a mammogram every 2 years, with the choice to continue getting them every year.
- Continue screening as long as the woman is in good health and expected to live 10 years or more.
If you have a family history of breast cancer or a personal health history that increases your risk (radiation exposure, genetic mutation), speak with your provider about starting mammograms earlier, or having additional tests, such as breast MRI or ultrasound. Many centers are now making use of digital and 3D mammograms, which are more sensitive than conventional mammography.

Guidelines for a clinical breast exam (completed by your healthcare provider) have changed. This exam is no longer recommended; as there is no clinical evidence to support that it will detect cancer early. Women should still be familiar with their normal breast tissue and report any changes in appearance, size, or feel of the tissue or nipples, or any nipple discharge to their health care provider.

In certain populations of women, MRI screening in addition to mammogram may be recommended. The American Cancer Society now recommends yearly breast MRI and mammogram for breast cancer screening for women who carry a known BRCA 1 or 2 mutation, those with a very strong family history of breast or ovarian cancer, and those who have had prior radiation treatment to the chest (for example, radiation as part of treatment for Hodgkin Lymphoma). Other populations of women who may benefit from MRI screening are those who have already had breast cancer, those with known lobular carcinoma in situ (LCIS), and those with very dense breasts, which may be difficult to visualize on mammograms. Decisions regarding how to screen for breast cancer (with mammograms or both mammogram and MRI) should be made between an individual and her healthcare provider, based on her individual breast cancer risk profile.

What are the signs of breast cancer?

Unfortunately, the early stages of breast cancer may not have any symptoms. This is why it is important to follow screening recommendations. As a tumor grows in size, it can produce a variety of symptoms including:

- Lump or thickening in the breast or underarm
- Change in size or shape of the breast
- Nipple discharge or the nipple turning inward
- Redness or scaling of the skin or nipple
- Ridges or pitting of the breast skin

These symptoms do not always signify the presence of breast cancer, but they should always be evaluated immediately by a healthcare professional.

How is breast cancer diagnosed?

Once a woman has symptoms suggestive of breast cancer or an abnormal screening mammogram, they will usually be referred for a diagnostic mammogram. A diagnostic mammogram is another set of x-rays with additional angles and close-up views. Often, an ultrasound will be performed during the same session. An ultrasound uses high-frequency sound waves to outline the suspicious areas of the breast. It is painless and can often distinguish between benign and malignant lesions.

Depending on the results of the mammograms and/or ultrasounds, your providers may recommend that you have a biopsy. A biopsy is the only way to know for sure if you have cancer because it allows your providers to get cells that can be examined under a microscope.

There are different types of biopsies; they differ with regard to how much tissue is removed. Some biopsies use a very fine needle, while others use thicker needles or even require a surgical procedure to remove more tissue. Your team of providers will decide which type of biopsy you need depending on your particular breast mass.

Once the tissue is removed, a pathologist will review the specimen. The pathologist can tell if the cells are cancerous or not. If the tumor does represent cancer, the pathologist will describe what type of tissue it arose from, how abnormal it looks (known as the grade), whether or not it is invading surrounding tissues, and whether or not the entire lump was removed during surgery/biopsy. The pathologist will also test the cancer cells for the presence of estrogen, progesterone, and HER-2 receptors. The presence of estrogen and progesterone receptors are important because cancers that have these receptors can be treated with hormonal therapies. HER-2 expression may help predict prognosis and allow for treatment with therapies directed specifically at HER-2. See Understanding Your Pathology Report for more information.
How is breast cancer staged?

In order to guide treatment and offer some insight into prognosis, breast cancer is staged into five different groups. This staging is done in a limited fashion before surgery, taking into account the size of the tumor on the mammogram and any evidence of spread to other organs that is picked up with other imaging modalities. It is done again after a surgical procedure that removes lymph nodes and allows a pathologist to examine the entire specimen. The staging system is very complex. A simplified version is described below, and the entire staging system is outlined at the end of this article.

- **Stage 0:** (called carcinoma in situ/non-invasive breast cancers)
  - *Lobular carcinoma in situ (LCIS)* refers to abnormal cells lining a gland in the breast. This is a risk factor for the future development of cancer, but this is not felt to represent cancer itself.
  - *Ductal carcinoma in situ (DCIS)* refers to abnormal cells lining a duct. Women with DCIS have an increased risk of getting invasive breast cancer in that breast. Treatment options are similar to patients with Stage I breast cancers.

- **Stage I:** early-stage breast cancer where the tumor is less than 2 cm and hasn't spread beyond the breast.

- **Stage II:** early-stage breast cancer in which the tumor is either less than 2 cm across and has spread to the lymph nodes under the arm; or the tumor is between 2 and 5 cm (with or without spread to the lymph nodes under the arm), or the tumor is greater than 5 cm and hasn't spread outside the breast.

- **Stage III:** locally advanced breast cancer in which the tumor is greater than 5 cm across and has spread to the lymph nodes under the arm; or the cancer is extensive in the underarm lymph nodes; or cancer has spread to lymph nodes near the breastbone or to other tissues near the breast.

- **Stage IV:** metastatic breast cancer in which cancer has spread outside the breast to other organs in the body.

Depending on the stage of your cancer, your provider may want additional tests to determine whether cancer has spread to any organs outside of the breast and surrounding lymph nodes. Nearly all women with a breast cancer diagnosis will need a chest x-ray and basic blood work. If you have stage III cancer, your provider may recommend other tests, such as CT scan and bone scan. Each case is unique and your providers will determine what is necessary to adequately stage your cancer.

How is breast cancer treated?

Treatments for breast cancer vary based on many individual factors, including cancer stage, age and overall health, and individual pathologic findings. Treatments for early-stage and advanced breast cancer are discussed separately in the upcoming sections of this article.

**Treatment for Early/Moderate Stage Breast Cancer**

Generally speaking, early/moderate-stage breast cancer refers to breast cancer that is stage 0-II. These cancers are less than 5 centimeters, can be removed surgically, and have not spread beyond the breast and regional lymph nodes.

Because of the potential risk to fertility associated with chemotherapy medications used to treat breast cancer, discuss *fertility preservation* options with your healthcare provider before starting treatment.

**Surgery**

Almost all women with early/moderate-stage breast cancer will have some type of surgery in the course of their treatment. The purpose of surgery in this setting is to remove as much of the cancer as possible. There are many different ways that the surgery can be performed. Some women will be candidates for what is called breast-conserving surgery (BCS). BCS may refer to a *lumpectomy*, during which the tumor and a portion of normal tissue are removed, or a segmental/partial mastectomy, during which a larger piece of tissue, but not the whole breast, is removed. Many patients will also have surgical procedures to remove lymph nodes from the axilla (armpit). Any patient who has invasive breast cancer (any stage except stage 0) should have lymph nodes tested. This may be with a *sentinel lymph node biopsy*, when 1-2 lymph nodes are removed, or an *axillary dissection*, when many more nodes are removed, or both. The pathologist will review both the breast tissue removed during BCS and the lymph node tissue that is removed. They will create a report that includes the type of cancer cells that are seen, the size of the cancer, and the number of lymph nodes that have cancer in them. These factors will help to determine what further treatment may be needed.

In most cases, a woman who undergoes breast-conserving surgery will require radiation treatment to the remaining breast.
tissue. The reason for this is that radiation decreases the risk of the cancer recurring (coming back) in the breast tissue. Very large studies have shown that breast-conserving surgery and radiation are as effective as mastectomy (removal of the entire breast) for patients with early/moderate stage breast cancer. Many patients prefer BCS and radiation to mastectomy because BCS allows the patient to keep her breast. However, some women with early-stage breast cancer prefer mastectomy, and this is certainly another treatment option and a very personal decision.

**Modified radical mastectomy** refers to the removal of the entire breast, as well as the dissection of the lymph nodes under the arm. Many women who have modified radical mastectomies choose to undergo breast reconstruction. A patient who desires reconstruction should try to meet with a plastic surgeon before her mastectomy to discuss reconstruction options. Learn more about breast reconstruction.

**Chemotherapy**

Even when tumors are removed by surgery, microscopic cancer cells can be present and spread to distant sites in the body. In order to decrease a patient's risk of the cancer returning (called recurrence), many breast cancer patients are offered chemotherapy. **Chemotherapy** is the use of anti-cancer drugs that go throughout the entire body to eliminate cancer cells that have broken off from the breast tumor and spread. Many factors go into determining whether an individual patient should have chemotherapy. Generally, patients with higher stage disease need chemotherapy; however, chemotherapy can be beneficial even for patients with early-stage disease. Individual factors such as age, overall health, and biologic properties of a woman's breast tumor go into decisions regarding whether or not she should have chemotherapy. In some cases, the genetic makeup of the tumor may be used to determine the potential benefit of chemotherapy. Available tests to evaluate this include OncoType Dx and MammaPrint.

There are many different chemotherapy medicines, and they are usually given in combinations for 3 to 6 months after surgery for early/moderate stage breast cancer. Most chemotherapies used for breast cancer are given through a vein, so they need to be given in an oncology clinic/infusion center. Medications that are commonly used in early/moderate stage breast cancer treatment include adriamycin (doxorubicin), cyclophosphamide, taxanes (taxol and taxotere), methotrexate, and 5-FU. There are advantages and disadvantages to each of the different regimens that your medical oncologist will discuss with you. Based on your own health and side effects you may wish to avoid, you can work with your providers to choose the best regimen for you.

**Radiation**

Many patients with early/moderate stage breast cancer require radiation therapy. Radiation therapy refers to the use of high energy x-rays to kill cancer cells. As discussed previously, radiation therapy is recommended for nearly all early-stage breast cancer patients who have breast-conserving surgery. Radiation is important in reducing the risk of local recurrence. Your radiation oncologist can answer questions about the benefits, process, and side effects of radiation therapy in your particular case.

Patients having radiation usually need to come to a radiation therapy treatment center 5 days a week for up to 6 weeks to receive treatment. The treatment takes just a few minutes, and it is painless. Most patients having radiation for early/moderate stage breast cancer receive treatment to the whole breast for 4-5 weeks; the final 1-2 weeks of treatment usually involve a "boost" of radiation that is only delivered to the area in the breast where the tumor was. Some other regimens exist for delivering radiation for early/moderate-stage breast cancers. One approach includes giving more radiation per day to the whole breast so that the treatment takes only 4 weeks. Other approaches reduce the treatment time to 1 week (brachytherapy or Mammosite). Another technique may include radiation to the regional lymph nodes, which is thought to reduce recurrence. These techniques are only appropriate for certain patients. Your radiation oncologist will discuss the most appropriate course of treatment for your individual case.

**Hormone Therapy**

When the pathologist examines a tumor specimen, he or she may determine that the tumor is expressing estrogen (ER) and/or progesterone (PR) receptors. Patients whose tumors express these receptors may be candidates for therapy with estrogen-blocking medications. **Estrogen-blocking medications** include tamoxifen and a family of medications called aromatase inhibitors (anastrozole, letrozole, exemestane). These medications are delivered in pill form for 5 - 10 years after breast cancer surgery. They have been shown to drastically reduce your risk of recurrence if your tumor expresses estrogen receptors. They may be accompanied by side effects, however. When taking tamoxifen, patients may experience weight gain, hot flashes, and vaginal dryness and discharge. Taking tamoxifen may also increase the risk of serious medical issues, such as blood clots, stroke, and uterine cancer. Tamoxifen is generally used in pre-menopausal women.
Patients taking aromatase inhibitors (AIs) may experience bone or joint pain and are at increased risk for thinning of the bones (osteopenia or osteoporosis). Patients taking AIs should have bone density testing prior to starting treatment and periodically based on results and may require treatment for bone thinning. AIs have been used for post-menopausal women for some time. More recently it has been found that they can be effective in suppressing estrogen in pre-menopausal women when combined with a GnRH analog such as Lupron.

Targeted Therapy

Targeted therapies work more specifically than standard chemotherapy by targeting something specific to the cancer cells, often inhibiting some function that is necessary for cell division.

HER-2 is a receptor that is over-expressed in about 25% of breast cancers. These are referred to as HER2 positive breast cancers. These tumors grow faster and are more likely to spread, but there are also medications designed specifically to target the HER2 protein, giving these tumors an extra treatment option. The most common treatment for HER2 positive cancers is trastuzumab (Herceptin®), which may be given to treat the cancer or prevent it from recurring. In addition, neratinib (Nerlynx), ado-trastuzumab emtansine (Kadcyla) also treat certain early stage HER2 positive cancers.

Other targets are being studied and new medications are approved each year. One receptor, the mammalian target of rapamycin (mTor), is the target of a new class of agents, called mTor inhibitors, which includes a medication called everolimus. Another kind of targeted therapy is CD4/CD6 kinase inhibitors. Earlier stage breast cancer that are also hormone receptor positive (HR+) can be treated with the CD4/CD6 kinase inhibitors abemaciclib (Verzenio®) and ribociclib. Olaparib (Lynparza®) is a targeted therapy, called a PARP inhibitor, that can be used in women with breast cancer who also have a BRCA mutation. Your healthcare provider will advise you on which types of targeted therapies your tumor may be susceptible for treatment using targeted therapies.

Treatment for Advanced Breast Cancer

Advanced breast cancer is a term that is generally used to refer to breast cancers that are stage III or IV at the time of diagnosis or breast cancers that were stage 0-II at diagnosis and have recurred (come back) in other parts of the body. The treatments used in advanced breast cancer include surgery, radiation, chemotherapy, hormone therapy, and/or biologic therapies.

Surgery

There are many reasons that patients with advanced breast cancer may need to undergo surgery. Locally advanced (stage III) breast cancers are usually treated with a modified radical mastectomy. This refers to the removal of the entire breast, as well as dissection of the lymph nodes under the arm. In some cases, a woman with stage III breast cancer can receive chemotherapy to shrink the tumor before surgery. This is called neoadjuvant therapy. This may be done to allow breast-conserving surgery (removal of only the tumor and a small amount of breast tissue and not the whole breast) or to make the mastectomy surgery more feasible. This is a decision that can only be made with guidance from your surgical team. Your surgeon can discuss your options and the pros and cons of these surgical procedures. Many women who have modified radical mastectomies choose to undergo reconstruction. A patient who desires reconstruction should try to meet with a plastic surgeon before her mastectomy to discuss reconstruction options. Learn more about breast reconstruction.

Some women who are diagnosed with stage IV cancer, or women with early-stage cancer that has become metastatic, may also require modified radical mastectomy. At other times, women with stage IV disease may only undergo breast biopsy without a larger surgery. This may be done because the treatment team feels that medication therapy is required to manage the disease that is present and that surgery will not be beneficial for the patient and will further delay chemotherapy. In some cases, a patient with stage IV disease may be able to have surgery to remove tumors that have spread to other sites, (i.e. brain, spinal cord, and lungs) in order to relieve symptoms or control further spread of the cancer.

Radiation

Radiation therapy is the use of high-energy x-rays to kill cancer cells. There are a few ways that radiation therapy may be used for patients with advanced breast cancer. Some patients require radiation therapy to the breast or the chest wall after a modified radical mastectomy. Many patients having this treatment will also require radiation to the axilla (armpit) or supraclavicular (lower neck) regions. This radiation can be given at the same time as radiation to the breast or chest wall and is given with the goal of killing any cancer cells that may be in the patient’s lymph nodes. Generally, this radiation will require the patient to come for radiation treatments 5 days a week for 5-6 weeks. The radiation treatments themselves are painless, but skin irritation and fatigue can develop as the radiation course goes on.
Radiation in patients with advanced/metastatic breast cancer may also be palliative focused. This means the treatment is to relieve symptoms and quality of life. Palliative radiation therapy often targets an area where the cancer has metastasized such as the brain, bones or spine.

**Chemotherapy**

The term "advanced breast cancer" means that the cancer cells have spread beyond the original tumor into lymph nodes, the tissue surrounding the tumor or other areas of the body. In some cases, the cancer cells cannot be seen on radiology scans, but we suspect they may be traveling through the blood and lymphatic systems. In stage IV (metastatic) disease, these cells typically form tumors that can be seen on radiology scans and/or cause problems or symptoms for the patient. For this reason, the treatment for patients with advanced breast cancer must be "systemic" – meaning it can travel throughout the body. Systemic treatments include **chemotherapy**, **hormone therapy** and **targeted therapies**, including those targeting HER2 receptors. Surgery and radiation are local treatments, as they can only treat a specific area.

Treatment of advanced breast cancer varies from patient to patient. It requires discussion between patient and oncologist and consideration of many factors, including hormone receptor and HER2 status, prior treatments, the patient's other health conditions, goals of treatment, and balancing quality of life with treatment side effects. Your oncologist may prescribe one chemotherapy agent or a combination of agents. Sometimes a certain combination of medications will be given for several cycles. If they appear not to work or to stop working, your provider may recommend that the combination of medications be changed. Your provider may also give you a chemotherapy break if you have severe side effects from the medications.

Some patients with advanced breast cancers receive a certain, planned number of cycles of therapy. At the end of this number of cycles, the treatment is stopped. Some patients may have aggressive breast surgery (either breast-conserving surgery or modified radical mastectomy) either before or after chemotherapy. Other patients require chemotherapy for the rest of their lives. For these patients, breast cancer may become a chronic illness that never goes away; however, it can often be controlled for many, many years with medications that do not make the patient very sick. For these patients, one goal of treatment is for effective chemotherapy to be given while the patient maintains a good quality of life. Based on your own health, your personal values and wishes, and side effects you may wish to avoid, you can work with your providers to come up with the best regimen for your lifestyle.

There are many different chemotherapy medications, which can be given alone or in various combinations. Many chemotherapy medicines used for breast cancer are given through a vein, so they need to be given in an oncology clinic, although some can be given by mouth, in the form of a pill. Some of the standard chemotherapy agents that are used in the treatment of breast cancer include **adriamycin** (doxorubicin), **cyclophosphamide**, **methotrexate**, taxanes (taxol and taxotere), **capecitabine**, **fluorouracil**, **vinorelbine**, **eribulin**, **carboplatin**, **epirubicin**, and **ixabepilone**.

**Targeted Therapy**

Targeted therapies work more specifically than standard chemotherapy by targeting something specific to the cancer cells, often inhibiting some function that is necessary for cell division.

HER-2 is a receptor that is over-expressed in about 25% of breast cancers. These are referred to as HER2 positive breast cancers. These tumors may grow faster and are more likely to spread, but there are also medications designed specifically to target the HER2 protein, giving these tumors an extra treatment option. The most common treatment for HER2 positive cancers is **trastuzumab** (Herceptin®), which may be given to treat the cancer or prevent it from recurring. In addition, **neratinib** (Nerlynx), **ado-trastuzumab emtansine** (Kadcyla) also treat certain early stage HER2 positive cancers.

Other targets are being studied and new medications are approved each year. One receptor, the mammalian target of rapamycin (mTor), is the target of a new class of agents, called mTor inhibitor. **Everolimus** is an mTOR inhibitor used in the treatment of advanced breast cancer. Advanced breast cancer that is also hormone receptor-positive (HR+) can be treated with the CD4/CD6 kinase inhibitors **palbociclib** (Ibrance®), and **ribociclib** (Kisqali®). **Olaparib** (Lynparza®) is a targeted therapy, called a PARP inhibitor, that can be used in women with breast cancer who also have a BRCA mutation. **Alpelisib** (Piqray®) is a PI3K inhibitor targeted therapy used in the treatment of advanced breast cancer. It is estimated that 30-40% of all breast cancers have a mutation of the PIK3CA gene.

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targeted therapies.

Hormone Therapy

When the pathologist examines a tumor specimen, he or she may determine that the tumor is expressing estrogen and/or progesterone receptors. Patients whose tumors express estrogen receptors are candidates for therapy with estrogen-blocking medications. Estrogen-blocking medications include tamoxifen and a family of medications called aromatase inhibitors (anastrozole, letrozole, exemestane).

These can be given for 5 - 10 years after an advanced breast cancer diagnosis or can be used as a treatment for metastatic cancers. They can be very effective at preventing new growth of breast cancer; however, they may be accompanied by side effects. When taking tamoxifen, patients may experience weight gain, hot flashes, and vaginal discharge. Taking tamoxifen may also increase the risk of serious medical issues, such as blood clots, stroke, and uterine cancer. Patients taking aromatase inhibitors may experience bone or joint pain and are at increased risk for thinning of the bones (osteopenia or osteoporosis). Patients taking aromatase inhibitors should have bone density testing prior to starting treatment and periodically based on results and may require treatment for bone thinning.

Clinical Trials

Clinical trials are extremely important in furthering our knowledge of this disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your healthcare provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the OncoLink Clinical Trials Matching Service.

Follow-up Care and Survivorship

Once you have been treated for breast cancer, you need to be closely followed for a recurrence. At first, you will have follow-up visits every 3-6 months. The longer you are free of disease, the less often you will have to go for checkups. After 5 years, you may only see your provider once a year. For those treated with breast-conserving surgery, you will be instructed to have a mammogram about 12 months after the completion of treatment. Women treated with a single mastectomy should have yearly mammograms of the remaining breast. Because having had breast cancer is a risk factor for getting it again, having mammograms is extremely important.

If you are taking tamoxifen, it is important that you get a pelvic exam each year and report any abnormal vaginal bleeding to your provider. Tamoxifen can increase your risk of uterine cancer and vaginal bleeding can be a symptom of uterine cancer. If you are taking an aromatase inhibitor, your bone health will be monitored.

If you are having symptoms of recurrence your provider will instruct you to have other tests done such as blood tests, including tumor marker studies and liver function tests, CT scans, bone scan, MRI, biopsy and/or x-rays. It is important to speak with your provider regarding any new symptoms or side effects you are having to determine if these symptoms could be related to recurrence, long-term side effects of treatment, or another unrelated health issue. Some may ask why they do not have these tests periodically to monitor for recurrence. Studies have found that the tests do not find a recurrence any sooner than a patient develops symptoms and these tests do not improve outcomes, so they are not recommended.

There are a number of long-term side effects and issues related to treatment for breast cancer. Here are some of the more common side effects and issues that you may have to manage after treatment for breast cancer:

- Lymphedema is the buildup of fluid in the arm in which you had lymph nodes removed. Lymphedema causes swelling, tightness and sometimes pain in the affected arm. Your provider can refer you to a physical therapist who specializes in working with lymphedema. You should be educated about reducing your risk of developing lymphedema.
- Body image issues are common in those treated with surgery. The removal of part or even the whole breast may leave a woman feeling as though she is disfigured. Speak with your provider regarding the options you have including speaking with a therapist who specializes in body image issues, a reconstructive surgeon and someone who provides and fits specialty bras and inserts.
- Sexuality can be impacted and is related to the body image issues a woman might face. A woman may be left with scars
from surgery, lack of sensation in the breast(s) and may even be affected by chronic chest pain. Speak with your provider and partner to determine ways to manage sexuality issues.

- Fertility is a topic that should be discussed prior to starting treatment since some treatments may affect a woman’s ability to have a baby. If after treatment a woman would like to conceive, you may wish to see an oncofertility specialist to evaluate your fertility.

Fear of recurrence, the financial impact of cancer treatment, employment issues, and coping strategies are common emotional and practical issues experienced by breast cancer survivors. Your healthcare team can identify resources for support and management of these practical and emotional challenges faced during and after cancer.

Cancer survivorship is a relatively new focus of oncology care. With some 17 million cancer survivors in the US alone, there is a need to help patients transition from active treatment to survivorship. What happens next, how do you get back to normal, what should you know and do to live healthy going forward? A survivorship care plan can be a first step in educating yourself about navigating life after cancer and helping you communicate knowledgeably with your healthcare providers. Create a survivorship care plan today on OncoLink.

**Resources for More Information**

**After Breast Cancer Diagnosis**

Provides free, personalized information and one-to-one support to people affected by breast cancer – patients, families, and friends.

http://www.abcdbreastcancersupport.org/

**BreastCancer.org**

A nonprofit organization dedicated to providing the most reliable, complete, and up-to-date information about breast cancer.

http://www.breastcancer.org/

**FORCE**

Facing Our Risk of Cancer Empowered is a nonprofit organization for women who are at high risk of getting breast or ovarian cancers due to their family history and genetic status.

http://www.facingourrisk.org/index.php

**Linda Creed Breast Cancer Foundation**

The mission of Linda Creed is to fight breast cancer with heart through community-based education and referral, support, advocacy and direct service for those who need it.

http://www.lindacreed.org/

**Living Beyond Breast Cancer**

Provides support and education for patients, family members, and healthcare professionals.

http://www.lbbc.org/

**Sister’s Network, Inc.**

Aims to increase local and national attention to the impact that breast cancer has had on the African American community.

http://www.sistersnetworkinc.org/

**Susan G. Komen Breast Cancer Foundation**

The world’s largest nonprofit source of funding for the fight against breast cancer, investing in research, community health outreach, advocacy and programs in more than 30 countries.

http://ww5.komen.org/
**Young Survival Coalition**
A global organization dedicated to the critical issues unique to young women who are diagnosed with breast cancer.
http://www.youngsurvival.org/

**Mothers Supporting Daughters with Breast Cancer (MSDBC)**
A support organization for mothers whose daughters have breast cancer.
www.mothersdaughters.org/

**Sharsheret**
A national not-for-profit organization supporting young women and their families, of all Jewish backgrounds, facing breast cancer. Our mission is to offer a community of support to women diagnosed with breast cancer or at increased genetic risk, by fostering culturally-relevant individualized connections with networks of peers, health professionals, and related resources.
http://www.sharsheret.org/about

**Hope for Two**
An international, non-profit organization for women diagnosed with cancer during pregnancy.
Http://www.hopefortwo.org

**Appendix: Complete Breast Cancer Staging**
Stage Information for Breast Cancer (AJCC Staging System 8th Edition 2016)

<table>
<thead>
<tr>
<th>Primary Tumor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>Tis (DCIS)</td>
<td>Ductal carcinoma in situ</td>
</tr>
<tr>
<td>Tis (Paget's)</td>
<td>Paget's disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget's disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget's disease should still be noted</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor less than or equal to 20mm or less in greatest dimension</td>
</tr>
<tr>
<td>T1mi</td>
<td>Tumor less than or equal to 1mm in greatest dimension</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor greater than 1mm but less than or equal to 5mm in greatest dimension</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor greater than 5mm but less than or equal to 10mm in greatest dimension</td>
</tr>
<tr>
<td>T1c</td>
<td>Tumor greater than 10mm but less than or equal to 20mm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor greater than 20mm but less than or equal to 50mm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor greater than 50mm in greatest dimension</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules).</td>
</tr>
<tr>
<td>T4a</td>
<td>Extension to the chest wall, not including only pectoralis muscles adherence/invasion</td>
</tr>
<tr>
<td>T4b</td>
<td>Ulcerations and/or ipsilateral satellite nodules and/or edema (including peau d’orange) of the skin, which do not meet the criteria for inflammatory carcinoma</td>
</tr>
<tr>
<td>-----</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>T4c</td>
<td>Both T4a and T4b</td>
</tr>
<tr>
<td>T4d</td>
<td>Inflammatory carcinoma</td>
</tr>
</tbody>
</table>

### Lymph Node \( (N) \) Clinical Description

| cNX | Regional lymph nodes cannot be assessed.                                                                                                    |
| cN0 | No regional lymph node metastasis                                                                                                           |
| cN1 | Metastases to movable ipsilateral level I, II axillary lymph node(s)                                                                         |
| cN2 | Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matter; or in clinically detected ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases |
| cN2a| Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another or to other structures.                                     |
| cN2b| Metastases only in clinically detected ipsilateral internal mammary nodes and in the absence of clinically evident I, II axillary lymph node metastases |
| cN3 | Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement |
| cN3a| Metastasis in ipsilateral infraclavicular lymph node(s)                                                                                       |
| cN3b| Metastasis in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)                                                        |
| cN3c| Metastasis in ipsilateral supraclavicular lymph node(s)                                                                                      |

### Lymph Node \( (N) \) Pathologic Description

<p>| pNX | Regional lymph nodes cannot be assessed                                                                                                     |
| pN0 | No regional lymph node metastasis histologically                                                                                              |
| pN0(i-)| No regional lymph node metastases histologically, negative IHC                                                                               |
| pN0(i+)| Malignant cells in regional lymph nodes no greater than 0.2mm                                                                               |
| pN0(mol-)| No regional lymph node metastases histologically, negative molecular findings                                                              |
| pN0(mol+)| Positive molecular findings, but not regional node metastases detected by histology                                                        |
| pN1 | Micrometastases; or metastases in 1-3 axillary lymph nodes and/or internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected |
| pN1mi| Micrometastases greater than 0.2mm but not greater than 2.0mm                                                                               |
| pN1a | Metastases in 1-3 axillary lymph nodes, at least one metastases greater than 2.0mm                                                            |</p>
<table>
<thead>
<tr>
<th>pN1b</th>
<th>Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN1c</td>
<td>Metastases in 1-3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected</td>
</tr>
<tr>
<td>pN2</td>
<td>Metastases in 4-9 axillary lymph nodes or in clinically detected internal mammary lymph nodes in absence of axillary node metastases</td>
</tr>
<tr>
<td>pN2a</td>
<td>Metastases in 4-9 axillary nodes with at least one tumor deposit greater than 2mm</td>
</tr>
<tr>
<td>pN2b</td>
<td>Metastases in clinically detected internal mammary lymph nodes in the absence of axillary lymph node metastases</td>
</tr>
<tr>
<td>pN3</td>
<td>Metastases in ten or more axillary lymph nodes; or in infraclavicular (level III axillary) lymph nodes; or in clinically detected ipsilateral internal mammary lymph nodes in the presence of one or more positive level I, II axillary lymph nodes; or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected; or in ipsilateral supraclavicular lymph nodes</td>
</tr>
<tr>
<td>pN3a</td>
<td>Metastases in ten or more axillary lymph nodes (at least one tumor deposit greater than 2.0 mm); or metastases to the infraclavicular (level III axillary) lymph nodes</td>
</tr>
<tr>
<td>pN3b</td>
<td>Metastases in clinically detected ipsilateral internal mammary lymph nodes in the presence of one or more positive axillary lymph nodes; or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected</td>
</tr>
<tr>
<td>pN3c</td>
<td>Metastasis in ipsilateral supraclavicular lymph nodes</td>
</tr>
</tbody>
</table>

### Distant Metastases (M)

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
</tr>
<tr>
<td>cM0(i+)</td>
</tr>
<tr>
<td>cM1</td>
</tr>
<tr>
<td>pM1</td>
</tr>
</tbody>
</table>

After a T stage, N stage, and M stage has been defined, these factors are put together to determine the overall cancer stage:

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T0</td>
<td>N1mi</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1mi</td>
<td>M0</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Stage</th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
<th>M0</th>
<th>M1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IIA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2</td>
<td></td>
<td></td>
<td>N1</td>
<td></td>
<td></td>
<td>M0</td>
<td></td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td>N1</td>
<td>N2</td>
<td></td>
<td>M0</td>
<td></td>
</tr>
<tr>
<td>Stage IIIB</td>
<td></td>
<td>T4</td>
<td>T4</td>
<td>N0</td>
<td>N1</td>
<td></td>
<td>M0</td>
<td></td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>Any T</td>
<td></td>
<td></td>
<td>N3</td>
<td></td>
<td></td>
<td>M0</td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td></td>
<td></td>
<td>Any N</td>
<td></td>
<td></td>
<td>M1</td>
<td></td>
</tr>
</tbody>
</table>

**Histologic grade (Invasive)**

GX: Grade cannot be assessed

G1: Low combined histologic grade

G2: Intermediate combined histologic grade

G3: High combined histologic grade

**Histologic Grade (DCIS-Nuclear Grade)**

GX: Grade cannot be assessed

G1: Low nuclear grade

G2: Intermediate nuclear grade

G3: High nuclear grade

**Histopathologic Type**

**In situ Carcinomas**

Ductal carcinoma in situ

Paget's disease

**Invasive Carcinomas**

Not otherwise specified (NOS)

Ductal

Inflammatory

Medullary, NOS

Medullary with lymphoid stroma
Mucinous
Papillary (predominantly micropapillary pattern)
Tubular
Lobular
Paget's disease and infiltrating
Undifferentiated
Squamous cell
Adenoid cystic
Secretory
Cribriform

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