

Understanding a Breast Cancer Diagnosis

Types of Breast Cancer

There are several types of breast cancer. The type of breast cancer you have depends on where in the breast it started and other factors.

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Breast Cancer Grade and Other Tests

Doctors use information from your breast biopsy to learn a lot of important things about the exact kind of breast cancer you have.

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Stages and Outlook (Prognosis)

If you have been diagnosed with breast cancer, tests will be done to find out the extent (stage) of the cancer. The stage of a cancer helps determine how serious the cancer is

and how best to treat it.

- Stages of Breast Cancer
- Breast Cancer Survival Rates

Questions to Ask About Your Breast Cancer

You can take an active role in your breast cancer care by learning about your cancer and its treatment and by asking questions. Get a list of key questions here.

- Questions to Ask Your Doctor About Breast Cancer
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Types of Breast Cancer

There are many types of breast cancer. The most common types are ductal carcinoma in situ, invasive ductal carcinoma, and invasive lobular carcinoma.

The type of breast cancer is determined by the specific cells in the breast that are affected. Most breast cancers are **carcinomas**. Carcinomas are tumors that start in the epithelial cells that line organs and tissues throughout the body. Sometimes, an even more specific term is used. For example, most breast cancers are a type of carcinoma called **adenocarcinoma**, which starts in cells that make up glands (glandular tissue). Breast adenocarcinomas start in the ducts (the milk ducts) or the lobules (milk-producing glands).

There are other, less common, types of breast cancers, too, such as **sarcomas**, **phyllodes**, **Paget disease**, and **angiosarcomas** which start in the cells of the muscle, fat, or connective tissue.

Sometimes a single breast tumor can be a combination of different types. And in some very rare types of breast cancer, the cancer cells may not form a lump or tumor at all.

When a biopsy is done to find out the specific type of breast cancer, the pathologist will also check if the cancer has spread into the surrounding tissues. The following terms are used to describe the extent of the cancer:

- In situ breast cancers have not spread.
- Invasive or infiltrating cancers have spread (invaded) into the surrounding breast tissue.

Common kinds of breast cancer

The most common kinds of breast cancer are carcinomas, and are named based on where they form and how far they have spread.

These general kinds of breast cancer below can be further described with the terms outlined above.

In situ cancers

Ductal carcinoma in situ (DCIS; also known as *intraductal carcinoma*) is a non-invasive or pre-invasive breast cancer. See <u>Ductal Carcinoma in Situ (DCIS)</u> for more information.

Lobular carcinoma in situ (LCIS) may also be called lobular neoplasia. This breast change is not a cancer, though the name can be confusing. In LCIS, cells that look like cancer cells are growing in the lobules of the milk-producing glands of the breast, but they don't grow through the wall of the lobules. See <u>Lobular Carcinoma in Situ (LCIS)</u> for more information.

Invasive (infiltrating) breast cancer

Breast cancers that have spread into surrounding breast tissue are known as invasive breast cancer. There are many different kinds of invasive breast cancer, but the most common are called **invasive ductal carcinoma** and **invasive lobular carcinoma**. See Invasive Breast Cancer for more information.

Less common types of breast cancer

Inflammatory breast cancer

<u>Inflammatory breast cancer</u> is an uncommon type of invasive breast cancer. It accounts for about 1% to 5% of all breast cancers.

Paget disease of the nipple

<u>Paget disease of the nipple</u> starts in the breast ducts and spreads to the skin of the nipple and then to the areola(the dark circle around the nipple). It is rare, accounting for

only about 1-3% of all cases of breast cancer.

Phyllodes tumor

Phyllodes tumors are rare breast tumors. They develop in the connective tissue (stroma) of the breast, in contrast to carcinomas, which develop in the ducts or lobules. Most are benign, but there are others that are malignant (cancer). See Phyllodes Tumors of the Breastfor more information.

Angiosarcoma

Sarcomas of the breast are rare making up less than 1% of all breast cancers. <u>Angiosarcoma</u> starts in cells that line blood vessels or lymph vessels. It can involve the breast tissue or the skin of the breast. Some may be related to prior radiation therapy in that area.

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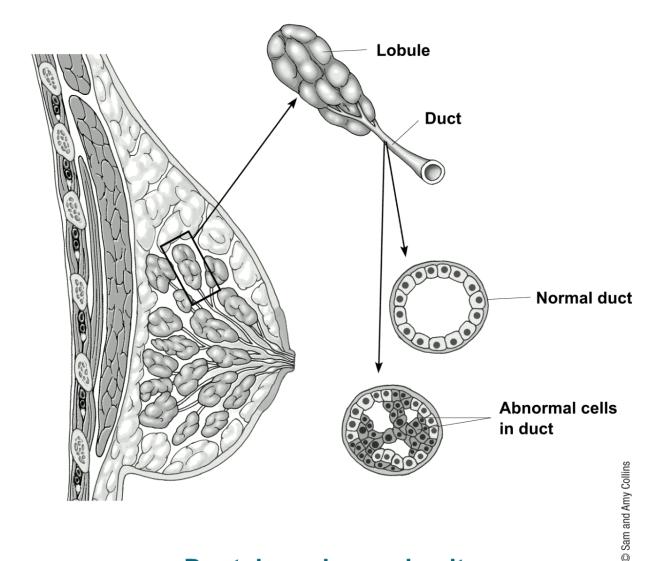
Ductal Carcinoma In Situ (DCIS)

About 1 in 5 new breast cancers will be DCIS or ductal carcinoma in situ. Nearly all women with this early stage of breast cancer can be cured.

Ductal carcinoma in situ(DCIS), is also called intraductal carcinoma and Stage 0 breast cancer. DCIS is a non-invasive or pre-invasive breast cancer. This means the cells that line the ducts have changed to cancer cells but they have not spread through the walls of the ducts into the nearby breast tissue.

Because DCIS hasn't spread into the breast tissue around it, it can't spread (metastasize) beyond the breast to other parts of the body.

DCIS is considered a pre-cancer because sometimes it can become an invasive cancer. This means that over time, DCIS may spread out of the duct into nearby tissue, and could metastasize (spread). Right now, though, there's no good way to know for sure which will become invasive cancer and which ones won't. So almost all women with DCIS will be treated.



Ductal carcinoma in situ

Learn about treatment for ductal carcinoma in situ.

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Invasive Breast Cancer (IDC/ILC)

Breast cancers that have spread into surrounding breast tissue are known as invasive breast cancer. There are different kinds of invasive breast cancer. Some kinds are more common than others.

Invasive (infiltrating) ductal carcinoma (IDC)

This is the most common type of breast cancer. About 8 of 10 invasive breast cancers are invasive (or infiltrating) ductal carcinomas (IDC).

IDC starts in the cells that line a milk duct in the breast, breaks through the wall of the duct, and grows into the nearby breast tissues. At this point, it may be able to spread (metastasize) to other parts of the body through the lymph system and bloodstream.

Invasive lobular carcinoma (ILC)

Invasive lobular carcinoma (ILC) starts in the milk-producing glands (lobules). Like IDC, it can spread (metastasize) to other parts of the body. About 1 invasive breast cancer in 10 is an ILC. Invasive lobular carcinoma may be harder to detect on physcial exam as well as imaging, like mammograms, than invasive ductal carcinoma. And compared to other kinds of invasive carcinoma, about 1 in 5 women with ILC might have cancer in both breasts.

Special types of invasive breast cancer

There are some special types of breast cancer that are sub-types of invasive carcinoma. They are much less common than the breast cancers listed named above and each typically make up fewer than 5% of all breast cancers. These are often named after features seen when they are viewed under the microscope, like the ways the cells are arranged.

Some of these may have a better prognosis than standard invasive infiltrating ductal carcinoma. These include:

- Adenoid cystic (or adenocystic) carcinoma
- Low-grade adenosquamous carcinoma (this is a type of metaplastic carcinoma)
- Medullary carcinoma
- Mucinous (or colloid) carcinoma
- Papillary carcinoma
- Tubular carcinoma

Some sub-types have the same or maybe worse prognoses than standard invasive infiltrating ductal carcinoma. These include:

- Metaplastic carcinoma (most types, including spindle cell and squamous, except low grade adenosquamous carcinoma)
- Micropapillary carcinoma
- Mixed carcinoma (has features of both invasive ductal and lobular)

In general, all of these sub-types are still treated like standard invasive infiltrating ductal carcinoma.

Learn about <u>treatments for invasive breast cancer</u>.

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Inflammatory Breast Cancer

Inflammatory breast cancer (IBC) is rare. It differs from other types of breast cancer in its symptoms, outlook, and treatment. Symptoms include **breast swelling, purple or red color of the skin,** and **pitting or thickening of the skin of the breast** so that it may look and feel **like an orange peel**. Often, a lump is not felt. If you have any of these symptoms, it does not mean that you have IBC, but you should see a doctor right away.

What is inflammatory breast cancer?

Inflammatory breast cancer (IBC) has some symptoms of inflammation like swelling and redness. But infection or injury do not cause IBC or the symptoms. IBC symptoms are caused by cancer cells blocking lymph vessels in the skin.

How is inflammatory breast cancer different from other types of breast cancer?

Inflammatory breast cancer differs (IBC) from other types of breast cancer in several key ways:

- IBC doesn't look like a typical breast cancer. It often does not cause a breast lump, and it might not show up on a mammogram. This makes it harder to diagnose.
- IBC tends to occur in younger women (at an average age of 52 versus 57 for more

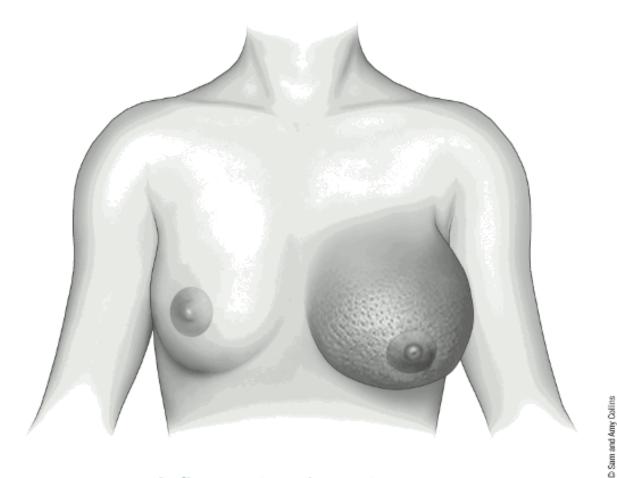
common forms of breast cancer).

- African-American women appear to be at higher risk of IBC than white women.
- IBC is more common among women who are overweight or obese.
- IBC also tends to be more aggressive—it grows and spreads much more quickly—than more common types of breast cancer.
- IBC is always at a locally advanced stage when it's first diagnosed because the breast cancer cells have grown into the skin. (This means it at least stage IIIB.)
- In about 1 of every 3 cases, IBC has already spread (metastasized) to distant parts of the body when it is diagnosed. This makes it harder to treat successfully.

What are the signs and symptoms of inflammatory breast cancer?

Inflammatory breast cancer (IBC) causes a number of signs and symptoms, most of which develop quickly (withing 3-6 months), including:

- Thickening (edema/swelling) of the skin of the breast
- Redness involving more than one-third of the breast
- Pitting or thickening of the skin of the breast so that it may look and feel like an orange peel
- A retracted or inverted nipple
- One breast looking larger than the other because of swelling
- One breast feeling warmer and heavier than the other
- A breast that may also be tender, painful or itchy



Inflammatory breast cancer

Tenderness, redness, warmth, and itching are also common symptoms of a breast infection or inflammation, such as mastitis if you're pregnant or breastfeeding. Because these problems are much more common than IBC, your doctor might at first suspect infection as a cause and treat you with antibiotics.

This may be a good first step, but if your symptoms don't get better in 7 to 10 days, more tests need to be done to look for cancer. The possibility of IBC should be considered more strongly if you have these symptoms and are not pregnant or breastfeeding, or have been through menopause.

IBC grows and spreads quickly, so the cancer may have already spread to nearby lymph nodes by the time symptoms are noticed. This spread can cause swollen lymph nodes under your arm or above your collar bone. If the diagnosis is delayed, the cancer can spread to lymph nodes in your chest or to distant sites.

If you have any of these symptoms, it does not mean that you have IBC, but you should

see a doctor right away. If treatment with antibiotics is started, you'll need to let your doctor know if it doesn't help, especially if the symptoms get worse or the affected area gets larger. Ask to see a specialist (like a breast surgeon) or you might want to get a second opinion if you're concerned.

How is inflammatory breast cancer diagnosed?

Imaging tests

If inflammatory breast cancer (IBC) is suspected, one or more of the following imaging tests may be done:

- Mammogram
- Breast ultrasound
- MRI (magnetic resonance imaging) scan
- CT (computed tomography) scan
- PET (positron emission tomography) scan

Sometimes a photo of the breast is taken to help record the amount of redness and swelling before starting treatment.

Biopsy

Breast cancer is diagnosed by a biopsy, taking out a small piece of the breast tissue and looking at it in the lab. Your physical exam and other tests may show findings that are "suspicious for" IBC, but only a biopsy can tell for sure that it is cancer.

Tests on biopsy samples

The cancer cells in the biopsy sample will be *graded* based on how abnormal they look. They will also be tested for certain proteins that help decide which treatments will be helpful.

The cells are tested for <u>hormone receptors</u>. Women whose breast cancer cells contain hormone receptors are likely to benefit from treatment with hormone therapy drugs.

Cancer cells are also tested to see if they contain too much of a protein called HER2/neu (often just called HER2) or too many copies of the gene for that protein. If they do, the woman may be helped by certain drugs that target HER2.

Stages of inflammatory breast cancer

All Inflammatory breast cancers start as **Stage IIIB** since they involve the skin. If the cancer has spread to lymph nodes around the collarbone or inside the chest, it's **stage IIIC**. Cancer that has spread outside the breast and nearby lymph nodes is **stage IV**.

For more information, , read about <u>breast cancer staging</u>.

Survival rates for inflammatory breast cancer

Inflammatory breast cancer (IBC) is considered an aggressive cancer because it grows quickly, is more likely to have spread at the time it's found, and is more likely to come back after treatment than other types of breast cancer. The outlook is generally not as good as it is for other types of breast cancer.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. Many other factors can affect a person's outlook, such as age, general health, treatment received, and how well the cancer responds to treatment. Your doctor can tell you how the numbers below may apply to you, as he or she is familiar with your situation.

These survival rates are based on people diagnosed years ago. Improvements in treatment since then may result in a more favorable outlook for people now being diagnosed with inflammatory breast cancer.

These numbers are based on data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database, for patients who were diagnosed with inflammatory breast cancer between 1990 and 2008.

Median survival is the length of time for half of the patients in a group to have died. By definition, half of the patients in that group are still alive. It is important to remember that the median is just a kind of average used by researchers. No one is "average" and many people have much better outcomes than the median. Also, people with inflammatory breast cancer can die of other things, and these numbers don't take that into account.

- The median survival rate for people with stage III inflammatory breast cancer is about 57 months.
- The median survival rate for people with stage IV inflammatory breast cancer is

How is inflammatory breast cancer treated?

Inflammatory breast cancer (IBC) that has not spread outside the breast or nearby lymph nodes is stage IIIB or IIIC. In most cases, treatment is chemotherapy to try to shrink the tumor, followed by surgery to remove the cancer. Radiation is given after surgery, and, in some cases, more treatment may be given after radiation.

IBC that has spread to other parts of the body (stage IV) may be treated with chemotherapy, hormone therapy, and/or with drugs that targets HER2.

For details, see treatment of inflammatory breast cancer.

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Angiosarcoma of the Breast

What is angiosarcoma of the breast?

Angiosarcoma is rare cancer that starts in the cells that line blood vessels or lymph vessels. It's sometimes a complication of previous radiation treatment to the breast. It can also occur in the affected arms of women with lymphedema, but this is not common. (Lymphedema is swelling that can develop after surgery or radiation therapy to treat breast cancer.) It can cause skin changes and/or a lump in the breast.

How is angiosarcoma treated?

Angiosarcomas tend to grow and spread quickly. Treatment usually includes <u>surgery</u> to remove the breast (mastectomy), and is generally the same as for other sarcomas.

Typically the axillary lymph nodes are not removed. For more information on sarcomas, see soft tissue sarcomas.

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Paget Disease of the Nipple

Paget disease of the nipple is a rare type of breast cancer involving the skin of the nipple. Paget disease starts in the breast ducts and spreads to the skin of the nipple and then to the areola, the dark circle around the nipple. Paget disease usually affects only one nipple. It's usually linked to either ductal carcinoma in situ (DCIS) or infiltrating ductal carcinoma.

Paget disease can look very similar to eczema (very dry skin) of the nipple. Your physician may try to treat this as eczema first, and if it does not improve, recommend a biopsy.

What are the signs and symptoms of Paget disease of the nipple?

The skin of the nipple and areola often looks crusted, scaly, and red. There may be blood or yellow fluid coming out of the nipple. Sometimes the nipple looks flat or inverted. It also might burn or itch.

How is Paget disease of the nipple diagnosed?

Most people with Paget disease of the nipple also have tumors in the same breast. One or more of the following imaging tests may be done to check for other breast changes:

- Diagnostic mammogram
- Breast ultrasound
- MRI (magnetic resonance imaging) scan

Paget disease of the nipple is diagnosed by a <u>biopsy</u>, removing a small piece of the breast tissue and looking at it in the lab. In some cases, the entire nipple may be removed. Only a biopsy can tell for sure that it is cancer.

How is Paget disease of the nipple treated?

Paget disease can be treated by removing the entire breast (<u>mastectomy</u>) or <u>breast-conserving surgery</u> followed by whole-breast <u>radiation therapy</u>.

If no lump is felt in the breast tissue, and your biopsy results show the cancer has not spread, the outlook (prognosis) is excellent.

If the cancer has spread (is invasive), the outlook is not as good, and the cancer will be staged and treated like any other invasive ductal carcinoma.

Breast Cancer Hormone Receptor Status

Breast cancer cells taken out during a <u>biopsy</u> or <u>surgery</u> will be tested to see if they have certain proteins that are estrogen or progesterone receptors. When the hormones estrogen and progesterone attach to these receptors, they fuel the cancer growth. Cancers are called hormone receptor-positive or hormone receptor-negative based on whether or not they have these receptors (proteins). Knowing the hormone receptor status is important in deciding treatment options.

What are estrogen and progesterone receptors?

Receptors are proteins in or on cells that can attach to certain substances in the blood. Normal breast cells and some breast cancer cells have receptors that attach to the hormones estrogen and progesterone, and depend on these hormones to grow.

Breast cancer cells may have one, both, or none of these receptors.

- **ER-positive:** Breast cancers that have estrogen receptors are called *ER-positive* (or ER+) cancers.
- **PR-positive**: Breast cancers with progesterone receptors are called *PR-positive* (or PR+) cancers.

Keeping these receptors from attaching to the hormones can help keep the cancer from growing and spreading. There are drugs that can be used to do this.

Why is knowing hormone receptor status important?

Knowing the hormone receptor status of your cancer helps doctors decide how to treat it. If your cancer has one or both of these hormone receptors, hormone therapy drugs can be used to either lower estrogen levels or stop estrogen from acting on breast cancer cells. This kind of treatment is helpful for hormone receptor-positive breast cancers, but it doesn't work on tumors that are hormone receptor-negative (both ER-and PR-negative).

All invasive breast cancers should be tested for both of these hormone receptors either on the biopsy sample or when the tumor is removed with surgery. About 2 of 3 breast cancers have at least one of these receptors. This percentage is higher in older women than in younger women. DCIS should be checked for hormone receptors, too.

What do the hormone receptor test results mean?

A test called an immunohistochemistry or IHC is used most often to find out if cancer cells have estrogen and progesterone receptors. The test results will help guide you and your cancer care team in making the best treatment decisions.

Test results will give you your hormone receptor status. It will say a tumor is hormone receptor-positive if at least 1% of the cells tested have estrogen and/or progesterone receptors. Otherwise the test will say the tumor is hormone receptor-negative.

Hormone receptor-positive (or hormone-positive) breast cancer cells have either estrogen (ER) or progesterone (PR) receptors. These breast cancers can be treated with <u>hormone therapy drugs</u> that lower estrogen levels or block estrogen receptors. This includes cancers that are ER-negative but PR-positive. Hormone receptor-positive cancers tend to grow more slowly than those that are hormone receptor-negative. Women with hormone receptor-positive cancers tend to have a better outlook in the short-term, but these cancers can sometimes come back many years after treatment.

Hormone receptor-negative (or hormone-negative) breast cancers have neither estrogen nor progesterone receptors. Treatment with hormone therapy drugs is not helpful for these cancers. These cancers tend to grow faster than hormone receptor-positive cancers. If they come back after treatment, it's often in the first few years. Hormone receptor-negative cancers are more common in women who have not yet gone through menopause.

Triple-negative breast cancer cells don't have estrogen or progesterone receptors and also don't make too much of the protein called <u>HER2</u>. These cancers tend to be more common in younger women and in women who are African-American or Hispanic/Latina. Triple-negative breast cancers grow and spread faster than most other types of breast cancer. Because the cancer cells don't have hormone receptors, hormone therapy is not helpful in treating these cancers. And because they don't have too much HER2, drugs that target HER2 aren't helpful, either. Chemotherapy can still be useful.

Triple-positive cancers are ER-positive, PR-positive, and HER2-positive. These cancers can be treated with hormone drugs as well as drugs that target HER2.

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Breast Cancer HER2 Status

Some women have breast tumors with higher levels of a protein known as HER2/neu – these are called HER2-positive breast cancers.

What is HER2/neu and what does it mean?

HER2/neu (often just shortened to HER2) is a growth-promoting protein on the outside of all breast cells. Breast cancer cells with higher than normal levels of HER2 are called HER2-positive. These cancers tend to grow and spread faster than other breast cancers. Women newly diagnosed with invasive breast cancers should be tested for HER2. It's important to know your "HER2 status" because HER2-positive cancers are much more likely to benefit from treatment with drugs that target the HER2 protein.. Ask your doctor about your HER2 status and what it means for you.

How are breast tumors tested for HER2?

A biopsy or surgery sample of the cancer is usually tested with either immunohistochemical stains (IHC) or Fluorescent in situ hybridization (FISH).

See <u>Testing Biopsy and Cytology Specimens</u> for cancer and <u>Understanding Your Pathology Report: Breast Cancer</u>to get more details about these tests.

What do the test results mean?

The results of HER2 testing will guide you and your cancer care team in making the best treatment decisions.

Many breast cancer specialists think that the FISH test is more accurate than IHC. However, it is more expensive and takes longer to get the results. Often the IHC test is done first.

- If the result is 0 or 1+, the cancer is considered **HER2-negative**. They do not respond to treatment with drugs that target HER2.
- If the result is 3+, the cancer is **HER2-positive**. They are usually treated with drugs that target HER2.

 If the result is 2+, the HER2 status of the tumor is not clear and is called "equivocal." This means that the HER2 status needs to be tested with FISH to clarify the result.

Triple-negative breast tumors don't have too much HER2 and also don't have <u>estrogen</u> <u>or progesterone receptors</u>. They are HER2-, ER-, and PR-negative. These cancers are more common in younger women and in African-American or Hispanic/Latina women. Triple-negative breast cancers grow and spread more quickly than most other types of breast cancer. Because the cancer cells don't have hormone receptors, hormone therapy is not helpful in treating these cancers. Because they don't have too much HER2, drugs that target HER2 aren't helpful, either. <u>Chemotherapy</u> can still be useful, though.

Triple-positive breast tumorsare HER2-, ER-, and PR-positive. These cancers are treated with hormone drugs as well as drugs that target HER2.

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Breast Cancer Gene Expression Tests

Tests that look at the patterns of certain genes (sometimes called *gene expression profiling*) can help predict if some early-stage (stage 1 or 2) breast cancers are likely to come back after initial treatment. Doctors can use this information to know which women will most likely benefit from chemotherapyafter breast surgery.

What are gene expression tests?

Looking at the patterns of a number of different genes at the same time can help predict if certain stage 1 or 2 breast cancers are likely to come back after initial treatment. Tests like these are part of what's being called "personalized medicine" – learning more about your cancer to specially tailor your treatment.

The **Oncotype DX**[®] and the **MammaPrint**[®] are examples of tests that look at different sets of breast cancer genes. And there are more tests in development.

How are the tests done?

Oncotype DX[®]: The Oncotype DX test is used for small <u>hormone receptor-positive</u> <u>tumors</u> that have not spread to more than 3 lymph nodes, but it may be used for more advanced tumors, too. It can also be used for <u>DCIS</u> (<u>ductal carcinoma in situ or stage 0</u> <u>breast cancer</u>).

This test looks at a set of 21 genes in cancer cells from tumor biopsy samples to get a "recurrence score," which is a number between 0 and 100. The score reflects the risk of the breast cancer coming back (recurring) in the next 10 years and how likely you will benefit from getting chemotherapy.

- A lower score means a low risk of recurrence. Women with low-recurrence scores would probably not benefit from chemotherapy.
- An intermediate score means an intermediate risk of recurrence. Women with
 intermediate-recurrence scores may have a small benefit from chemotherapy and
 should discuss the options, risks and benefits of chemotherapy with their doctor.
 Research is being done to see who in the intermediate group will benefit from
 chemotherapy.
- A high score means a high risk of recurrence. Women with high-recurrence

scores are likely to benefit from chemotherapy to help decrease the chance of the cancer coming back.

MammaPrint[®]: This test can be used to help determine how likely breast cancers are to recur in a distant part of the body after treatment. It can be used in any type of breast cancer that's small (stage 1 or 2) and has spread to no more than 3 lymph nodes. Hormone and HER2 status are assessed as part of this test.

The test looks at 70 different genes to determine if the cancer is at low risk or high risk of coming back (recurring) in the next 10 years. The test results come back as either "low risk" or "high risk."

What do the test results mean?

Gene expression testing (gene profiling) can help predict which women will most likely benefit from chemotherapy after breast surgery. (This is called adjuvant chemotherapy.) Hormone therapy is a standard treatment for hormone receptor-positive breast cancers, but it's not always clear when to use chemotherapy. These tests can help guide that decision.

Still, these tests cannot tell any one woman for certain if her cancer will come back with or without chemotherapy. Many doctors use these tests (along with other information) to help make decisions about offering chemotherapy. Keep in mind that these tests aren't needed in all cases. For instance, if you have a fast-growing or a stage 4 breast cancer, you don't need these tests because you should get chemotherapy as part of standard treatment.

These tests are now being looked at in large <u>clinical trials</u> to better understand how and when to best use them. In the meantime, women might want to ask their doctors if these tests might be useful for them.

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Breast Cancer: Ploidy and Cell Proliferation

Finding out more information about the DNA in the breast cancer cells can help predict how fast the cancer cells are dividing and growing.

What is ploidy and what does it mean?

The ploidy of cancer cells refers to the amount of DNA they contain.

- If there's a normal amount of DNA in the cells, they are said to be *diploid*. These cancers tend to grow and spread more slowly.
- If the amount of DNA is abnormal, then the cells are called *aneuploid*. These cancers tend to be more aggressive. (They tend to grow and spread faster.)

Tests of ploidy may help figure out long-term outcomes, but they rarely change treatment and are considered optional. They are not usually recommended as part of a routine breast cancer work-up.

What is cell proliferation?

Cell proliferation is how quickly a cancer cell copies its DNA and divides into 2 cells. If the cancer cells are dividing more rapidly, it means the cancer is faster growing or more aggressive.

The rate of cancer cell division can be estimated by doing a **Ki-67 test**. The *S-phase fraction* is the percentage of cells in a sample that are copying their DNA. DNA is copied when the cell is getting ready to divide into 2 new cells. If the S-phase fraction or Ki-67 labeling index is high, it means that the cancer cells are dividing more rapidly.

In some cases, Ki-67 testing to measure cell proliferation may be used to help plan treatment or estimate treatment outcomes. But test results vary depending on things like the lab doing the testing, the testing method, and what part of the tumor is tested. Still, there's a lot of interest in measuring tumor proliferation and standardizing testing methods, so this test is being used more often.

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Breast Cancer Grades

Knowing a breast cancer's grade is important to figure out how fast it's likely to grow and spread.

What is a breast cancer's grade?

Cancer cells are given a **grade** when they are removed from the breast and checked under a microscope. The **grade** is based on how much the cancer cells look like normal cells.

A lower grade number (1) usually means the cancer is slower-growing and less likely to spread.

A higher number (3) means a faster-growing cancer that's more likely to spread. The grade is used to help predict your outcome (prognosis) and help figure out what treatments might work best.

Three features are examined and each is assigned a score to determine the histologic grade. The scores are then added. This sum (between 3 and 9) is used to get a grade of 1, 2, or 3, which is noted on your pathology report. Sometimes words such as well differentiated, moderately differentiated, and poorly differentiated are used to describe the grade instead of numbers:

- Grade 1 or well differentiated (score 3, 4, or 5). The cells are slower-growing, and look more like normal breast tissue.
- Grade 2 or moderately differentiated (score 6, 7). The cells are growing at a speed of and look like cells somewhere between grades 1 and 3.
- **Grade 3 or poorly differentiated** (score 8, 9) . The cancer cells look very different from normal cells and will probably grow and spread faster.

Our information about <u>pathology reports</u> can help you understand details about your breast cancer.

Grading ductal carcinoma in situ (DCIS)

DCIS is graded only on how abnormal the cancer cells look. **Necrosis** (areas of dead or dying cancer cells) is also noted. If there is necrosis, it means the tumor is growing quickly.

The term **comedocarcinoma** is often used to describe DCIS with a lot of necrosis. If a breast duct is filled with a plug of dead and dying cells, the term **comedonecrosis** may be used. Comedocarcinoma and comedonecrosis are linked to a higher grade of DCIS.

See <u>Understanding Your Pathology Report: Ductal Carcinoma In Situ</u> for more on how DCIS is described.

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Stages of Breast Cancer

After a woman is diagnosed with breast cancer, doctors will figure out whether it has spread, and if so, how far. This is called *staging*. The stage of a cancer helps determine how serious the cancer is and how best to treat it.

What is staging?

Staging is the process of finding out how widespread the cancer is when it is found. The stage is one of the most important factors in deciding how to treat the cancer and determining how successful treatment might be.

To determine the cancer's stage after a breast cancer diagnosis, doctors must answer these questions:

- Is the cancer invasive or non-invasive?
- How big is the breast tumor? Has it grown into nearby areas?
- Has the cancer spread to nearby lymph nodes? If so, how many are involved?
- Has the cancer spread to other parts of the body?

Depending on the results of your history, physical exam, and biopsy, you might need more tests to help determine the stage, such as a chest x-ray, mammograms of both breasts, bone scans, CT scans, MRI, and/or PET scans. Blood tests may also be done to evaluate your overall health or to check for spread to certain organs.

See <u>Breast Cancer Early Detection and Diagnosis</u> for more information about tests to find breast cancer.

Understanding your breast cancer stage

Breast cancer is staged using the American Joint Committee on Cancer (AJCC) **TNM** system, which is based on 3 key pieces of information:

- The size of the breast tumor (**T**) and if it has grown into nearby areas
- Whether the cancer has reached nearby lymph nodes (N)
- Whether the cancer has metastasized (spread to other parts of the body) (M)

Numbers or letters after T, N, and M provide more details about each of these factors. Higher numbers mean the cancer is more advanced. Once a person's T, N, and M categories have been determined, sometimes after surgery, this information is combined in a process called stage grouping to assign an overall stage.

The earliest stage cancers are called stage 0 (carcinoma in situ), and then range from stages I (1) through IV (4). Some of the stages have sub stages with the letters A, B, and C.

As a rule, the lower the number, the less the cancer has spread. A higher number, such as stage IV (4), means a more advanced cancer. And within a stage, an earlier letter means a lower (and often better) stage. Cancers with similar stages tend to have a similar outlook and are often treated in much the same way.

The staging system in the table below uses the *pathologic stage*. It is based on the results of physical exam, biopsy, imaging tests, and the results of surgery. This is likely to be more accurate than *clinical staging*, which only considers the tests done *before*

surgery.

Breast cancer staging can be complex. If you have any questions about your stage, please ask your doctor to explain it to you in a way you understand. (An explanation of the TNM system also follows the stage table below.)

cancer of the breast. Many consider DCIS the earliest form of breast cancer. In DCIS, cancer cells are still within a duct and have not invaded deeper into the surrounding fatty breast tissue. Paget disease of the nipple (without an underlying tumor mass) is also stage 0. In all cases the cancer has not spread to lymph nodes or distant sites. Stage IA T1, N0, M0 The tumor is 2 cm (about 3/4 of an inch) or less across (T1) and has not spread to lymph nodes (N0) or distant sites (M0). Stage IB T0 or T1, N1mi, M0 The tumor is 2 cm or less across (or is not found) (T0 or T1) with micrometastases in 1 to 3 axillary lymph nodes (the cancer in the underarm lymph nodes is greater than 0.2mm across and/or more than 200 cells but is not larger than 2 mm)(N1mi). The cancer has not spread to distant sites (M0). Stage IIA T0 or T1, N1 (but not N1mi), M0: T1 or T0) and either: It has spread to 1 to 3 axillary (underarm) lymph nodes, with the cancer in the lymph nodes larger than 2 mm across (N1a), OR Tiny amounts of cancer are found in internal mammary lymph nodes (nodes near the breast bone) on sentinel lymph node biopsy (N1b), OR It has spread to 1 to 3 axillary lymph nodes and to internal mammary lymph nodes (found on sentinel lymph node biopsy) (N1c). The cancer has not spread to distant sites (M0). OR T2, N0, M0 The tumor is larger than 2 cm but less than 5 cm (about 2 inches) across (T2) but hasn't spread to			
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			the lymph nodes (N0). The cancer has not spread

		to distant sites (M0).
Stage IIB	T2, N1, M0	The tumor is larger than 2 cm but less than 5 cm across (T2). It has spread to 1 to 3 axillary lymph nodes and/or tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy (N1). The cancer hasn't spread to distant sites (M0).
	OR	
	T3, N0, M0	The tumor is larger than 5 cm across but does not grow into the chest wall or skin (T3). The cancer has not spread to the lymph nodes (N0) or to distant sites (M0).
Stage IIIA	T0 to T2, N2, M0	The tumor is not more than 5 cm across (or cannot be found) (T0 to T2). It has spread to 4 to 9 axillary lymph nodes, or it has enlarged the internal mammary lymph nodes (N2). The cancer hasn't spread to distant sites (M0).
	OR	
	T3, N1 or N2, M0	The tumor is larger than 5 cm across but does not grow into the chest wall or skin (T3). It has spread to 1 to 9 axillary nodes, or to internal mammary nodes (N1 or N2). The cancer hasn't spread to distant sites (M0).
Stage IIIB	T4, N0 to N2, M0	 The tumor has grown into the chest wall or skin (T4), and one of the following applies: It has not spread to the lymph nodes (N0). It has spread to 1 to 3 axillary lymph nodes and/or tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy (N1). It has spread to 4 to 9 axillary lymph nodes, or it has enlarged the internal mammary lymph nodes (N2). The cancer hasn't spread to distant sites (M0). Inflammatory breast cancer is classified as T4d and is at least stage IIIB. If it has spread to many nearby lymph nodes (N3) it could be stage IIIC, and if it has spread to distant lymph nodes or
Stage IIIC	any T, N3, M0	organs (M1) it would be stage IV. The tumor is any size (or can't be found), and one of the following applies:

		 Cancer has spread to 10 or more axillary lymph nodes (N3). Cancer has spread to the lymph nodes under the collar bone (infraclavicular nodes) (N3). Cancer has spread to the lymph nodes above the collar bone (supraclavicular nodes) (N3). Cancer involves axillary lymph nodes and has enlarged the internal mammary lymph nodes (N3). Cancer has spread to 4 or more axillary lymph nodes, and tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy (N3). The cancer hasn't spread to distant sites (M0).
Stage IV	any T, any N, M1	The cancer can be any size (any T) and may or may not have spread to nearby lymph nodes (any N). It has spread to distant organs or to lymph nodes far from the breast (M1). The most common sites of spread are the bones, liver, brain, or lungs.

Details of the TNM staging system

The TNM staging system classifies cancers based on 3 areas called the T, N, and M categories:

T categories for breast cancer

The letter T followed by a number from 0 to 4 describes the main (primary) tumor's size and spread to the skin or to the chest wall under the breast. Higher T numbers mean a larger tumor and/or wider spread to tissues near the breast.

TX: Primary tumor cannot be assessed.

T0: No evidence of primary tumor.

Tis: Carcinoma in situ (DCIS, LCIS, or Paget disease of the nipple with no associated tumor mass)

T1 (includes T1a, T1b, and T1c): Tumor is 2 cm (3/4 of an inch) or less across.

T2: Tumor is more than 2 cm but not more than 5 cm (2 inches) across.

T3: Tumor is more than 5 cm across.

T4 (includes T4a, T4b, T4c, and T4d): Tumor of any size growing into the chest wall or skin. This includes inflammatory breast cancer.

N categories for breast cancer

The letter N followed by a number from 0 to 3 indicates whether the cancer has spread to lymph nodes near the breast and, if so, how many lymph nodes are involved.

Lymph node staging for breast cancer is based on how the nodes look under the microscope, and has changed as technology has improved. Newer methods have made it possible to find smaller and smaller collections of cancer cells, but experts haven't been sure how much these tiny deposits of cancer cells affect outlook.

It's not yet clear how much cancer in the lymph node is needed to see a change in outlook or treatment. This is still being studied, but for now, a deposit of cancer cells must contain at least 200 cells or be at least 0.2 mm across (less than 1/100 of an inch) for it to change the N stage. An area of cancer spread that is smaller than 0.2 mm (or fewer than 200 cells) doesn't change the stage, but is recorded with abbreviations (i+ or mol+) that indicate the type of special test used to find the spread.

If the area of cancer spread is at least 0.2 mm (or 200 cells), but still not larger than 2 mm, it is called a *micrometastasis* (one mm is about the size of the width of a grain of rice). Micrometastases are counted only if there aren't any larger areas of cancer spread. Areas of cancer spread larger than 2 mm are known to affect outlook and do change the N stage. These larger areas are sometimes called *macrometastases*, but are more often just called *metastases*.

NX: Nearby lymph nodes cannot be assessed (for example, if they were removed previously).

N0: Cancer has not spread to nearby lymph nodes.

N0(i+): The area of cancer spread contains less than 200 cells and is smaller than 0.2 mm. The abbreviation "i+" means that a small number of cancer cells (called *isolated tumor cells*) were seen in routine stains or when a special type of staining technique, called *immunohistochemistry*, was used.

N0(mol+): Cancer cells cannot be seen in underarm lymph nodes (even using special stains), but traces of cancer cells were detected using a technique called *RT-PCR*. RT-PCR is a molecular test that can find very small numbers of cancer cells. (This test is not often used for finding breast cancer cells in lymph nodes because the results do not influence treatment decisions.)

N1: Cancer has spread to 1 to 3 axillary (underarm) lymph node(s), and/or tiny amounts of cancer are found in internal mammary lymph nodes (those near the breast bone) on sentinel lymph node biopsy.

N1mi: Micrometastases (tiny areas of cancer spread) in 1 to 3 lymph nodes under the arm. The areas of cancer spread in the lymph nodes are 2 mm or less across (but at least 200 cancer cells or 0.2mm across).

N1a: Cancer has spread to 1 to 3 lymph nodes under the arm with at least one area of cancer spread greater than 2 mm across.

N1b: Cancer has spread to internal mammary lymph nodes, but this spread could only be found on sentinel lymph node biopsy (it did not cause the lymph nodes to become enlarged).

N1c: Both N1a and N1b apply.

N2: Cancer has spread to 4 to 9 lymph nodes under the arm, or cancer has enlarged the internal mammary lymph nodes

N2a: Cancer has spread to 4 to 9 lymph nodes under the arm, with at least one area of cancer spread larger than 2 mm.

N2b: Cancer has spread to one or more internal mammary lymph nodes, causing them to become enlarged.

N3: Any of the following:

N3a: either:

Cancer has spread to 10 or more axillary lymph nodes, with at least one area of cancer spread greater than 2mm, OR

Cancer has spread to the lymph nodes under the collar bone (infraclavicular nodes), with at least one area of cancer spread greater than 2mm.

N3b: either:

Cancer is found in at least one axillary lymph node (with at least one area of cancer spread greater than 2 mm) and has enlarged the internal mammary lymph nodes, OR

Cancer has spread to 4 or more axillary lymph nodes (with at least one area of cancer spread greater than 2 mm), and tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy.

N3c: Cancer has spread to the lymph nodes above the collar bone (supraclavicular nodes) with at least one area of cancer spread greater than 2mm.

M categories for breast cancer

The letter M followed by a 0 or 1 indicates whether the cancer has spread to distant organs -- for example, the lungs or bones.

MX: Distant spread (metastasis) cannot be assessed.

M0: No distant spread is found on x-rays (or other imaging tests) or by physical exam.

cM0(i+): Small numbers of cancer cells are found in blood or bone marrow (found only by special tests), or tiny areas of cancer spread (no larger than 0.2 mm) are found in lymph nodes away from the underarm, collar bone, or internal mammary areas.

M1: Cancer has spread to distant organs (most often to the bones, lungs, brain, or liver).

References

American Joint Committee on Cancer. Breast. In: *AJCC Cancer Staging Manual*, 7th ed. New York: Springer; 2010: 347–369.

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Survival rates tell you what portion of people with the same type and stage of cancer are still alive a certain amount of time (usually 5 years) after they were diagnosed. They can't tell you how long you will live, but they may help give you a better understanding

about how likely it is that your treatment will be successful. . Some people will want to know the survival rates for their cancer type and stage, and some people won't. If you don't want to know, you don't have to.

What is a 5-year survival rate?

Statistics on the outlook for a certain type and stage of cancer are often given as 5-year survival rates, but many people live longer – often much longer – than 5 years. **The 5-year survival rateis the percentage of people who live** *at least* **5 years after being diagnosed with cancer.** For example, a 5-year survival rate of 90% means that an estimated 90 out of 100 people who have that cancer are still alive 5 years after being diagnosed.

Relative survival rates are a more accurate way to estimate the effect of cancer on survival. These rates compare women with breast cancer to women in the overall population. For example, if the 5-year relative survival rate for a specific type of cancer is 90%, it means that people who have that cancer are, on average, about 90% as likely as people who don't have that cancer to live for at least 5 years after being diagnosed.

But remember, the 5-year relative survival rates are estimates – your outlook can vary based on a number of factors specific to you.

Cancer survival rates don't tell the whole story

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they can't predict what will happen in any particular person's case. There are a number of limitations to remember:

- The numbers below are among the most current available. But to get 5-year survival rates, doctors have to look at people who were treated at least 5 years ago.
 As treatments are improving over time, women who are now being diagnosed with breast cancer may have a better outlook than these statistics show.
- The available statistics for breast cancer do not divide survival rates by all of the sub stages, such as IA and IB. The rates for these substages are likely to be close to the rate for the overall stage. For example, the survival rate for stage IA is likely to be slightly higher than that listed for stage I, while the survival rate for stage IB would be expected to be slightly lower.
- These statistics are based on the stage of the cancer when it was first diagnosed. They do not apply to cancers that come back later or spread, for example.

Many other factors can affect a person's outlook, such as age and health, the
presence of hormone receptors on the cancer cells, the treatment received, and
how well the cancer responds to treatment.

Your doctor can tell you how these numbers may apply to you, as he or she is familiar with your particular situation.

Breast cancer survival rates, by stage

The outlook for women with breast cancer varies by the stage (extent) of the cancer. In general, the survival rates are better for women with earlier stage cancers. But remember, the outlook for each woman is specific to her circumstances. The numbers below come from the National Cancer Institute's SEER database, looking at people diagnosed with breast cancer between 2007 and 2013.

- The 5-year relative survival rate for women with stage 0 or stage I breast cancer is close to 100%.
- For women with stage II breast cancer, the 5-year relative survival rate is about 93%.
- The 5-year relative survival rate for stage III breast cancers is about 72%. But often, women with these breast cancers can be successfully treated.
- Breast cancers that have spread to other parts of the body are more difficult to treat and tend to have a poorer outlook. Metastatic, or stage IV breast cancers, have a 5year relative survival rate of about 22%. Still, there are often many treatment options available for women with this stage of breast cancer.

Remember, these survival rates are only estimates – they can't predict what will happen to any individual person. We understand that these statistics can be confusing and may lead you to have more questions. Talk to your doctor to better understand your specific situation.

Please note that these statistics are based on the previous version of AJCC staging. In that version stage II also included patients that would now be considered stage IB.

References

Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2014, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2014/, based on November 2016 SEER data submission, posted to the SEER web site, April 2017.

Questions to Ask Your Doctor About Breast Cancer

It's important to be able to have frank, open discussions with your cancer care team. They want to answer all of your questions, so that you can make informed treatment and life decisions.

Here are some questions that you can use to help better understand your cancer and your treatment options. Don't be afraid to take notes and tell the doctors or nurses when you don't understand what they're saying. You might want to bring another person with you when you see your doctor and have them take notes to help you remember what was said.

Not all of these questions will apply to you, but they should help get you started. Be sure to write down some questions of your own. For instance, you might want more information about recovery times or you may want to ask about nearby or online support groups where you can talk with other women going through similar situations. You may also want to ask if you qualify for any <u>clinical trials</u>.

Keep in mind that doctors aren't the only ones who can give you information. Other health care professionals, such as nurses and social workers, can answer some of your questions. To find out more about speaking with your health care team, see
The Doctor-Patient Relationship.

When you're told you have breast cancer

- Exactly what type of breast cancer do I have?
- How big is the cancer? Where exactly is it?
- Has the cancer spread to my lymph nodes or other organs?
- What's the <u>stage</u> of the cancer? What does that mean?
- Will I need any other tests before we can decide on treatment?
- Do I need to see any other doctors or health professionals?
- What is the hormone receptor status of my cancer? What does this mean?
- What is the HER2 status of my cancer? What does this mean?

- How do these factors affect my treatment options and long-term outlook (prognosis)?
- What are my chances of survival, based on my cancer as you see it?
- Should I think about genetic testing? What would the pros and cons of testing be?
- How do I get a copy of my pathology report?
- If I'm concerned about the costs and <u>insurance coverage</u> for my diagnosis and treatment, who can help me?

When deciding on a treatment plan

- How much experience do you have treating this type of cancer?
- Should I get a second opinion? How do I do that?
- What are my <u>treatment</u> choices?
- What treatment do you recommend and why?
- Should I think about taking part in a <u>clinical trial</u>?
- What would the goal of the treatment be?
- How soon do I need to start treatment?
- How long will treatment last? What will it be like? Where will it be done?
- What should I do to get ready for treatment?
- What risks or side effects are there to the treatments you suggest? Are there things
 I can do to reduce these side effects?
- How will treatment affect my daily activities? Can I still work fulltime?
- Will I lose my hair? If so, what can I do about it?
- Will I go through menopause as a result of the treatment? Will I be able to have children after treatment? Would I be able to breastfeed?
- What are the chances the cancer will come back (recur) after this treatment?
- What would we do if the treatment doesn't work or if the cancer comes back?
- What if I have transportation problems getting to and from treatment?

If you need surgery

- Is breast-conserving surgery (lumpectomy) an option for me? Why or why not?
- What are the pros and cons of breast-conserving surgery versus mastectomy?
- How many surgeries like mine have you done?
- Will you have to take out lymph nodes? If so, would you advise a sentinel lymph node biopsy? Why or why not?
- What side effects might lymph node removal cause?

- How long will I be in the hospital?
- Will I have stitches or staples at the surgery site? Will there be a drain (tube) coming out of the site?
- How do I care for the surgery site? Will I need someone to help me?
- What will my breasts look and feel like after my treatment? Will I have normal feeling in them?
- What will the scar look like?
- Is <u>breast reconstruction surgery</u> an option if I want it? What would it mean in my case?
- Can I have reconstruction at the same time as the surgery to remove the cancer?
 What are the pros and cons of having it done right away or waiting until later?
- What types of reconstruction might be options for me?
- Should I speak with a plastic surgeon about reconstruction options?
- Will I need a breast form (prosthesis), and if so, where can I get one?
- Do I need to stop taking any medications or supplements before surgery?
- When should I call your office if I'm having side effects?

During treatment

Once treatment begins, you'll need to know what to expect and what to look for. Not all of these questions may apply to you, but asking the ones that do may be helpful.

- How will we know if the treatment is working?
- Is there anything I can do to help manage side effects?
- What symptoms or side effects should I tell you about right away?
- How can I reach you on nights, holidays, or weekends?
- Will I need to change what I eat during treatment?
- Are there any limits on what I can do?
- Can I exercise during treatment? If so, what kind of exercise should I do, and how often?
- Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?
- Will I need special tests, such as imaging scans or blood tests? How often?

After treatment

Will I need a special diet after treatment?

- Are there any limits on what I can do?
- Am I at risk for lymphedema?
- What can I do to reduce my risk for lymphedema?
- What should I do if I notice swelling in my arm?
- What other symptoms should I watch for? What kind of exercise should I do now?
- What type of follow-up will I need after treatment?
- How often will I need to have follow-up exams, blood tests, or imaging tests?
- How will we know if the cancer has come back? What should I watch for?
- What will my options be if the cancer comes back?

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