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Understanding a Breast Cancer Diagnosis

If you've been diagnosed with breast cancer, you've probably heard a lot of different terms used to describe your cancer. Doctors use information from your breast biopsy to learn a lot of important things about the exact kind of cancer you have. You may also need more tests to get more details, such as the stage of the cancer or how fast it's growing.

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.

- Breast Cancer Grades
- Breast Cancer Ploidy and Cell Proliferation
- Breast Cancer Hormone Receptor Status
- Breast Cancer HER2 Status
- Breast Cancer Gene Expression Tests
- Other Breast Cancer Gene, Protein, and Blood Tests
- Understanding Your Pathology Report

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.

Imaging Tests to Find Out if Breast Cancer Has Spread

- Breast Cancer Stages
- 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

Connect with a breast cancer survivor

Reach To Recovery

The American Cancer Society Reach To Recovery® program connects people facing breast cancer – from diagnosis through survivorship – with trained volunteers who are breast cancer survivors. Our volunteers provide one-on-one support through our website and mobile app to help those facing breast cancer cope with diagnosis, treatment, side effects, and more.

Breast Cancer Grade

- What is a breast cancer's grade?
- Grading invasive breast cancer cells
- Grading ductal carcinoma in situ (DCIS)

Knowing a breast cancer's grade is important to understand 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 in the lab. The grade is based on how much the cancer cells look like normal cells. The grade is used to help predict your outcome (prognosis) and to help figure out what treatments might work best.

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

A **high grade number (grade 3)** means a faster-growing cancer that's more likely to spread.

An **intermediate grade number (grade 2)** means the cancer is growing faster than a grade 1 cancer but slower than a grade 3 cancer.

Grading invasive breast cancer cells

Three features of the invasive breast cancer cell are studied and each is given a score. The scores are then added to get a number between 3 and 9 that is used to get a grade of 1, 2, or 3, which is noted on your pathology report. Sometimes the terms *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 cells.
- 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>¹ can help you understand details about your breast cancer.

Grading ductal carcinoma in situ (DCIS)

DCIS is also graded on how abnormal the cancer cells look and has a similar grading system to that used for invasive breast cancer (see above).

- **Grade 1 or low grade DCIS**. The cells are growing slower, and look more like normal breast cells. These cells tend to have estrogen and progesterone receptors (ER-positive and PR-positive).
- **Grade 2 or intermediate grade**. The cells are growing at a speed of and look like cells somewhere between grades 1 and 3.
- Grade 3 or high grade. The cancer cells look very different from normal cells and are growing faster. These cells tend not to have estrogen and progesterone receptors (ER-negative and PR-negative). High grade DCIS is often more likely to turn into invasive breast cancer.

Necrosis (areas of dead or dying cancer cells) is also noted. If there is necrosis, it means the tumor is growing quickly. The term *comedo necrosis* may be used if a breast duct is filled with dead and dying cells. Comedo necrosis is often linked to a high grade of DCIS and has a higher chance of developing into invasive breast cancer.

See <u>Understanding Your Pathology Report: Ductal Carcinoma In Situ</u>² for more on how DCIS is described.

Hyperlinks

- 1. www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests/understanding-your-pathology-report.html
- 2. www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytologytests/understanding-your-pathology-report/breast-pathology/ductal-carcinoma-insitu.html

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Breast Cancer Ploidy and Cell Proliferation

- What is ploidy and what does it mean?
- What is cell proliferation?

Finding out more information about the <u>DNA</u>¹ 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 also 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 proliferation can be estimated by doing a **Ki-67 test**. In some cases, Ki-67 testing to measure cell proliferation may be used to help plan treatment or estimate treatment outcomes. But test results can vary depending on things like the lab doing the testing, the testing method, and what part of the tumor is tested.

Another way to determine cell division is the **S-phase fraction**, which is the percentage

of cells in a sample that are copying their DNA as it gets 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.

Hyperlinks

1. www.cancer.org/cancer/understanding-cancer/genes-and-cancer.html

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Breast Cancer Hormone Receptor Status

- What are estrogen and progesterone receptors?
- Why is knowing hormone receptor status important?
- How are breast tumors tested for hormone receptors?

What do the hormone receptor test results mean?

Breast cancer cells taken out during a <u>biopsy</u>¹ or <u>surgery</u>² 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 stimulate the cancer to grow. 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. Ask your doctor about your hormone receptor status and what it means for you.

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 need these hormones for the cells 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.
- Hormone receptor-positive: If the cancer cell has one or both of the receptors above, the term hormone-receptive positive (also called hormone-positive or HR+) breast cancer may be used.
- Hormone receptor-negative: If the cancer cell does not have the estrogen or the progesterone receptor, it's called hormone-receptor negative (also called hormone-negative or HR-).

Keeping the hormones estrogen and progesterone from attaching to the receptors can help keep the cancer from growing and spreading. There are <u>drugs that can be used to do this</u>³.

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 3 of 4 breast cancers have at least one of these receptors. This percentage is higher in older women than in younger women. DCIS should also be checked for hormone receptors.

How are breast tumors tested for hormone receptors?

A test called an **immunohistochemistry (IHC) test** 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.

What do the hormone receptor test results mean?

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 or both. These breast cancers can be treated with hormone therapy drugs that lower estrogen levels or block estrogen receptors. 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 no estrogen or 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 any or too much of the protein called HER2. These cancers tend to be more common in women younger than 40 years of age, who are Black, or who have a mutation in the *BRCA1* gene. 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. See <u>Triple-negative Breast Cancer</u>⁴ to learn more.

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.

Hyperlinks

- www.cancer.org/cancer/types/breast-cancer/screening-tests-and-earlydetection/breast-biopsy.html
- 2. <u>www.cancer.org/cancer/types/breast-cancer/treatment/surgery-for-breast-cancer.html</u>
- 3. <u>www.cancer.org/cancer/types/breast-cancer/treatment/hormone-therapy-for-breast-cancer.html</u>
- 4. <u>www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/triple-negative.html</u>

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Breast Cancer HER2 Status

- What is HER2 and what does it mean?
- How are breast tumors tested for HER2?
- What do the test results mean?

About 15% to 20% of breast tumors have higher levels of a protein known as HER2. These cancers are called **HER2-positive breast cancers**. Ask your doctor about your HER2 status and what it means for you.

What is HER2 and what does it mean?

HER2 is a protein that helps breast cancer cells grow quickly. Breast cancer cells with higher than normal levels of HER2 are called **HER2-positive**. These cancers tend to grow and spread faster than breast cancers that are HER2-negative, but are much

more likely to respond to treatment with <u>drugs that target the HER2 protein</u>¹.

All invasive breast cancers should be tested for HER2 either on the biopsy sample or when the tumor is removed with surgery.

How are breast tumors tested for HER2?

Either a test called an **immunohistochemistry (IHC) test** or **fluorescence in situ hybridization (FISH) test** is used to find out if cancer cells have a high level of the HER2 protein.

See <u>Testing Biopsy and Cytology Specimens for Cancer</u>² and <u>Understanding Your Pathology Report: Breast Cancer</u>³ 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.

It is not clear if one test is more accurate than the other, but FISH is more expensive and takes longer to get the results. Often the IHC test is done first.

- If the IHC result is 0, the cancer is considered **HER2-negative**. These cancers do not respond to treatment with drugs that target HER2.
- If the IHC result is 1+, the cancer is considered **HER2-negative**. These cancers do not usually respond to treatment with drugs that target HER2, but new research shows that certain HER2 drugs might help in some cases (see below).
- If the IHC 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.
- If the IHC result is 3+, the cancer is **HER2-positive**. These cancers are usually treated with drugs that target HER2.

Some breast cancers that have an IHC result of 1+ or an IHC result of 2+ along with a negative FISH test might be called **HER2-low** cancers. These breast cancers are still being studied but appear to benefit from <u>certain HER2-targeted drugs</u>⁴.

Triple-negative breast tumors don't have too much HER2 and also don't have estrogen or progesterone receptors. They are HER2-, ER-, and PR-negative. Hormone therapy

and drugs that target HER2 are not helpful in treating these cancers. See <u>Triple-negative Breast Cancer</u>⁵ to learn more.

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

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/breast-cancer/treatment/targeted-therapy-for-breast-cancer.html</u>
- 2. www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests.html
- 3. www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests/understanding-your-pathology-report/breast-pathology/breast-cancer-pathology.html
- 4. <u>www.cancer.org/cancer/types/breast-cancer/treatment/targeted-therapy-for-breast-cancer.html</u>
- 5. <u>www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/triple-negative.html</u>

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Breast Cancer Gene Expression Tests

- What do the test results mean?
- Testing options

Gene expression tests are a form of <u>personalized medicine</u>¹ - a way to learn more about your cancer and tailor your treatment.

These tests are done on breast cancer cells after surgery or biopsy to look at the patterns of a number of different genes. This process or test is sometimes called **gene expression profiling**.

What do the test results mean?

The patterns found can help predict if certain early-stage breast cancers are likely to come back after initial treatment.

Some gene expression testing/profiling can help predict which women will most likely benefit from <u>chemotherapy</u>² after breast surgery (adjuvant chemotherapy.) <u>Hormone therapy</u>³ 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.

These tests continue to be studied in large <u>clinical trials</u>⁴ to better understand how and when to best use them. In the meantime, ask your doctor if these tests might be useful for you.

Testing options

The Oncotype DX, MammaPrint, and Prosigna are examples of tests that look at different sets of breast cancer genes to see if chemotherapy is needed to help reduce the risk of cancer coming back (recurrence). More tests are in development. The type of test that's used will depend on your situation. Keep in mind that these tests are used for early-stage cancers, and testing isn't needed in all cases. For example, if breast cancer is advanced, it might be clear that chemotherapy is needed, even without gene expression testing.

Oncotype DX

The Oncotype DX test is used for stage I, II or IIIa hormone receptor-positive tumors that have not spread to more than 3 lymph nodes and are HER2 negative. It can also be used for DCIS (ductal carcinoma in situ or stage 0 breast cancer)⁵.

This test looks at a set of 21 genes in cancer cells from tumor biopsy or surgery 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 9 years if you are treated with hormone therapy alone and how likely you are to benefit from getting chemo after surgery.

For women who are older than 50 years and have no lymph nodes with cancer:

- A low score (0-25) means a low risk of recurrence. Most women with low-recurrence scores do not benefit from chemotherapy and have good outcomes when treated with hormone therapy.
- A high score (26-100) means a higher risk of recurrence. Women with highrecurrence scores are more likely to benefit from the addition of chemotherapy to hormone therapy to help lower the chance of the cancer coming back.

For women age 50 or younger and have no lymph nodes with cancer:

- A low score (0-15) means a low risk of recurrence. Most of these women with low-recurrence scores do not benefit from chemotherapy and have good outcomes when treated with hormone therapy.
- An intermediate score (16-25) means that some women in this group might have a small benefit from adding chemotherapy to hormone therapy to lower the risk of the cancer coming back. Talk to your doctor about options.
- A high score (26-100) means a higher risk of recurrence. Women with highrecurrence scores are more likely to benefit from the addition of chemotherapy to hormone therapy to help lower the chance of the cancer coming back.

For women age 50 or younger that have cancer in the lymph nodes:

- A low score (0-25) means a lower risk of recurrence, but women in this group might have a benefit from adding chemotherapy to hormone therapy. Another option might be <u>ovarian suppression along with tamoxifen or an aromatase</u> inhibitor⁶.
- A high score (26-100) means a higher risk of recurrence. Women in this group are more likely to benefit from the addition of chemotherapy to hormone therapy to help lower the chance of the cancer coming back.

MammaPrint

The MammaPrint 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 for any type of invasive breast cancer that's 5cm (about 2 inches) or smaller and has spread to no more than 3 lymph nodes. This test can be done regardless of a woman's age or the cancer's hormone or HER2 status.

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." This test is also being studied as a way to determine whether certain women might benefit from chemotherapy.

Prosigna

The Prosigna test can be used to predict the risk of recurrence in the next 10 years in women who have gone through menopause (postmenopausal) and whose invasive breast cancers are hormone receptor-positive and HER2-negative. It can be used to test early-stage cancers that have not spread to the lymph nodes, or early-stage cancers with no more than 3 positive lymph nodes.

The test looks at 50 genes and classifies the results as low, intermediate, or high risk.

Breast Cancer Index

The Breast Cancer Index test is done on your tumor sample from when you are first diagnosed. It can be used to predict the risk of recurrence in the 5 to 10 years after diagnosis in women whose invasive breast cancers are hormone receptor-positive and

have not spread to nearby lymph nodes or have not spread to more than 3 lymph nodes. It can also help predict who might benefit from hormone therapy for longer than 5 years.

The test looks at 11 genes and classifies the results as low or high risk.

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/precision-medicine.html
- 2. <u>www.cancer.org/cancer/types/breast-cancer/treatment/chemotherapy-for-breast-cancer.html</u>
- 3. <u>www.cancer.org/cancer/types/breast-cancer/treatment/hormone-therapy-for-breast-cancer.html</u>
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Other Breast Cancer Gene, Protein, and Blood Tests

Tests for certain proteins on tumor cells

- Molecular tests for gene changes
- Blood tests

Samples that have been collected during biopsies, bloodwork, or other tests are sent to a pathology lab. A pathologist, a doctor who uses lab tests to diagnose diseases such as cancer, will look at the samples and may do other special tests to help better classify the cancer. These tests can also help choose certain drugs that might work better for your cancer. This is sometimes called <u>precision or personalized medicine</u>¹ because it is precise (or specific) for the features of your cancer.

The results of these tests are described in a pathology report, which is usually available within a week or two. If you have any questions about your pathology results or any diagnostic tests, talk to your doctor. If needed, you can get a second opinion of your pathology report by having your tissue samples sent to a pathologist at another lab.

Tests for certain proteins on tumor cells

Lab tests might also be done to look for certain proteins on the cancer cells.

Hormone receptor proteins: All breast cancers are tested for hormone receptors (proteins). Specifically, the cancer is tested for estrogen receptor (ER) and progesterone receptor (PR). Read more at Breast Cancer Hormone Receptor Status.

HER2 protein: All invasive breast cancers are tested for the HER2 protein to see if too much is being made. If it is not clear how much HER2 protein is present, the breast cancer cells might then undergo molecular testing for gene changes to see how many copies of the HER2 gene are being made. For more information about the HER2 gene and protein see **Breast Cancer HER2 Status**.

PD-L1 protein: People with advanced or metastatic triple-negative breast cancer might have their cancer tissue tested for the **PD-L1** protein, which can show if the cancer is more likely to respond to treatment with certain <u>immunotherapy</u>² drugs along with chemotherapy.

Molecular tests for gene changes

In some cases, doctors may test for specific gene changes in the breast cancer cells that could mean certain <u>targeted drugs</u>³ or immunotherapy drugs might help treat the cancer.

These molecular tests can be done on tissue taken during a biopsy or surgery for breast cancer. If the biopsy sample is too small and all the molecular tests cannot be done, the testing may also be done on blood that is taken from a vein just like a regular blood draw. This blood contains the DNA from dead tumor cells (known as **circulating tumor DNA**, or **ctDNA**). Obtaining the tumor DNA through a blood draw is sometimes called a "liquid biopsy" and can have advantages over a standard needle biopsy, which can carry risks.

Some genes that might be tested for include:

- BRCA1 and BRCA2 mutations: For women with an advanced HER2-negative breast cancer, your doctor might test you (not your cancer cells) for a hereditary BRCA1 or BRCA2 mutation⁴ (gene change). If you have one of these gene changes, treatment with the targeted drugs, olaparib (Lynparza) or talazoparib (Talzenna) might be options.
- *PIK3CA* gene mutation: Cancer cells that have a certain form of the PI3K protein can help them grow. This protein comes from an abnormal *PIK3CA* gene change. If your breast cancer is hormone-receptor-positive and HER2-negative and the breast cancer cells show this specific gene change, the targeted drug alpelisib (Piqray) along with the hormone drug⁵ fulvestrant (Faslodex) might be used.
- *ESR1 gene mutations:* The *ESR1* gene contains the cell's instructions for the estrogen receptor (ER) protein. Mutations in this gene can make breast cancers less likely to be helped by some forms of hormone therapy. But for advanced breast cancer, the hormone drug elacestrant (Orserdu) may be helpful if the cancer cells have an *ESR1* mutation. This gene change can be tested for in a sample of your blood.
- MSI and MMR testing: Breast cancer cells might be tested to see if they show high levels of gene changes called microsatellite instability (MSI). Testing might also be done to see if the cancer cells have changes in any of the mismatch repair (MMR) genes (MLH1, MSH2, MSH6, and PMS2). Breast cancer cells that have a high level of microsatellite instability (MSI-H) or a defect in a mismatch repair gene (dMMR) might be treated with the immunotherapy drugs, pembrolizumab (Keytruda) or dostarlizumab (Jemperli).
- Tumor mutational burden (TMB): TMB is a measure of the number of gene mutations (changes) inside the cancer cells. Breast cancer cells that have many gene mutations (a high TMB) might be more likely to be recognized as abnormal and attacked by the body's immune system. If your breast cancer tissue is tested and found to have a high TMB (TMB-H), treatment with pembrolizumab (Keytruda) might be an option.

NTRK fusion genes: Some breast cancer cells might have changes in one of the NTRK genes. These gene changes can sometimes lead to cancer growth.
 Larotrectinib (Vitrakvi) and entrectinib (Rozlytrek) are drugs that target the proteins made by the abnormal NTRK genes and might be options for people with advanced breast cancer.

Blood tests

Blood tests are not used to diagnose breast cancer, but they can help to get a sense of a person's overall health. For example, they can be used to help determine if a person is healthy enough to have surgery or certain types of chemotherapy.

A **complete blood count (CBC)** looks at whether your blood has normal numbers of different types of blood cells. For example, it can show if you are anemic (have a low number of red blood cells), if you could have trouble with bleeding (due to a low number of blood platelets), or if you are at increased risk for infections (because of a low number of white blood cells). This test could be repeated regularly during treatment, as many cancer drugs can affect blood-forming cells of the bone marrow.

Blood chemistry tests can help find if some of your organs, such as the liver or kidneys are not working as well. For example, if cancer has spread to the bones, it might cause higher than normal levels of calcium and alkaline phosphatase. If breast cancer spreads to the liver, it can sometimes cause high levels of liver function tests, such as aspartate aminotransferase (AST) or alanine aminotransferase (ALT). Breast cancer does not spread to the kidneys, but if your bloodwork shows your kidneys are not working well, certain chemo drugs, like cisplatin, might not be used.

Breast cancer cells sometimes make substances called **tumor markers** that can be found in the blood. For breast cancer that has spread to other organs, tumor markers that might be checked include carcinoembryonic antigen (CEA), cancer antigen 15-3 (CA 15-3), and cancer antigen 27-29 (CA 27-29). Blood tests for these tumor markers are not used by themselves to diagnose or follow breast cancer.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/treatment-types/precision-medicine.html

- 2. www.cancer.org/cancer/types/breast-cancer/treatment/immunotherapy.html
- 3. <u>www.cancer.org/cancer/types/breast-cancer/treatment/targeted-therapy-for-breast-cancer.html</u>
- 4. <u>www.cancer.org/cancer/types/breast-cancer/risk-and-prevention/genetic-testing.html</u>
- www.cancer.org/cancer/types/breast-cancer/treatment/hormone-therapy-forbreast-cancer.html

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Imaging Tests to Look for Breast Cancer Spread

- Chest x-ray
- Computed tomography (CT) scan

- Magnetic resonance imaging (MRI) scan
- Ultrasound
- Positron emission tomography (PET) scan
- Bone scan

If you have been diagnosed with breast cancer, you might need more imaging tests. Your doctor will talk with you about which of these tests you may need.

Imaging tests use x-rays, magnetic fields, sound waves, or radioactive substances to create pictures of the inside of your body. Imaging tests might be done for a number of reasons including:

- To look at suspicious areas that might be cancer
- To learn how far cancer might have spread
- To help determine if treatment is working
- To look for possible signs of cancer coming back after treatment

Chest x-ray

A chest x-ray¹ may be done to see if the cancer has spread to your lungs.

Computed tomography (CT) scan

A <u>CT scan</u>² uses x-rays to make detailed cross-sectional images of your body. Instead of taking 1 or 2 pictures, like a regular x-ray, a CT scanner takes many pictures and a computer then combines them to show a slice of the part of your body being studied. This test is most often used to look at the chest and/or belly (abdomen) to see if breast cancer has spread to other organs, like the lungs or liver.

CT-guided needle biopsy: If a suspected area of cancer is deep within your body, a CT scan might be used to guide a biopsy needle into this area to get a tissue sample to check for cancer.

Magnetic resonance imaging (MRI) scan

Like CT scans, MRI scans³ show detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. This test can be used to look at the breasts or other parts of the body, such as the brain or spinal cord to look for

possible cancer spread.

Ultrasound

<u>Ultrasound</u>⁴ (ultrasonography) uses sound waves to create an image on a video screen. A small microphone-like instrument called a transducer that gives off sound waves is moved over the skin surface and picks up the echoes as they bounce off tissues. A computer turns these echoes into an image on the screen. An ultrasound can be done over a breast or in the underarm area, or even the liver.

Positron emission tomography (PET) scan

For a <u>PET scan</u>⁵, a slightly radioactive form of sugar (known as FDG) is injected into the blood and collects mainly in cancer cells.

PET/CT scan: Often a PET scan is combined with a CT scan using a special machine that can do both at the same time. This lets the doctor compare areas of higher radioactivity on the PET scan with a more detailed picture on the CT scan.

Bone scan

A <u>bone scan</u>⁶ can help show if the cancer has spread to your bones. A small amount of low-level radioactive material is injected into the blood and collects mainly in abnormal areas of bone. It can show all of the bones of your body at the same time and can find small areas of cancer spread not seen on plain x-ray.

Hyperlinks

- 1. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/imaging-radiology-tests-for-cancer.html</u>
- 2. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ct-scan-for-cancer.html</u>
- 3. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/mri-for-cancer.html
- 4. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ultrasound-for-cancer.html
- 5. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/nuclear-medicine-

scans-for-cancer.html

6. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/nuclear-medicine-scans-for-cancer.html</u>

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Breast Cancer Stages

- How is the stage determined?
- Details of the TNM staging system
- Examples using the full staging system

After someone is diagnosed with breast cancer, doctors will try to figure out if it has spread, and if so, how far. This process is called **staging**. The stage of a cancer describes how much cancer is in the body. It helps determine how serious the cancer is and how best to <u>treat</u>¹ it. Doctors also use a cancer's stage when talking about <u>survival</u> statistics.

The earliest stage breast cancers are stage 0 (carcinoma in situ). It then ranges from

stage I (1) through IV (4). As a rule, the lower the number, the less the cancer has spread. A higher number, such as stage IV, means cancer has spread more. And within a stage, an earlier letter means a lower stage. Although each person's cancer experience is unique, cancers with similar stages tend to have a similar outlook and are often treated in much the same way.

How is the stage determined?

The staging system most often used for breast cancer is the American Joint Committee on Cancer (AJCC) **TNM system**. The most recent AJCC system, effective January 2018, has both clinical and pathologic staging systems for breast cancer:

- The **pathologic stage** (also called the**surgical stage**) is determined by examining tissue removed during an operation.
- Sometimes, if surgery is not possible right away or at all, the cancer will be given a **clinical stage** instead. This is based on the results of a physical exam, biopsy, and imaging tests. The clinical stage is used to help plan treatment. Sometimes, though, the cancer has spread further than the clinical stage estimates, and may not predict the patient's outlook as accurately as a pathologic stage.

In both staging systems, 7 key pieces of information are used:

- The extent (size) of the tumor (T): How large is the cancer? Has it grown into nearby areas?
- The spread to nearby lymph nodes (N): Has the cancer spread to nearby lymph nodes? If so, how many?
- The spread (metastasis) to distant sites (M): Has the cancer spread to distant organs such as the lungs or liver?
- Estrogen Receptor (ER) status: Does the cancer have the protein called an estrogen receptor?
- Progesterone Receptor (PR) status: Does the cancer have the protein called a progesterone receptor?
- HER2 status: Does the cancer make too much of a protein called HER2?
- Grade of the cancer (G): How much do the cancer cells look like normal cells?

In addition, Oncotype Dx® Recurrence Score results may also be considered in the stage in certain situations.

Once all of these factors have been determined, this information is combined in a process called **stage grouping** to assign an overall stage. For more information see Cancer Staging².

Details about the first three factors (the TNM categories) are below. However, the addition of information about ER, PR, and HER2 status along with grade has made stage grouping for breast cancer more complex than for other cancers. Because of this, it is best to ask your doctor about your specific stage and what it means.

Details of the TNM staging system

Numbers or letters after T, N, and M provide more details about each of these factors. Higher numbers mean the cancer is more advanced. The categories below use the pathologic (surgical) definitions.

T categories for breast cancer

T followed by a number from 0 to 4 describes the main (primary) tumor's size and if it has 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, or Paget disease of the breast 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

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 gotten better. Newer methods have made it possible to find smaller and smaller groups of cancer cells, but experts haven't been sure how much these tiny deposits of cancer cells influence 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 influence 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 fewer 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.

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

N1mi: Micrometastases (tiny areas of cancer spread) in the lymph nodes under the arm. The areas of cancer spread in the lymph nodes are at least 0.2mm across, but not larger than 2mm.

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 on the same side as the cancer, 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 2 mm,

OR

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

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 to the internal mammary lymph nodes on sentinel lymph node biopsy.

N3c: Cancer has spread to the lymph nodes above the collarbone (supraclavicular

nodes) on the same side of the cancer with at least one area of cancer spread greater than 2 mm.

M categories for breast cancer

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

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, collarbone, or internal mammary areas.

M1: Cancer has spread to distant organs (most often to the bones, lungs, brain, or liver) as seen on imaging tests or by physical exam, and/or a biopsy of one of these areas proves cancer has spread and is larger than 0.2mm.

Examples using the full staging system

Because there are so many factors that go into stage grouping for breast cancer, it's not possible to describe here every combination that might be included in each stage. The many different possible combinations mean that two women who have the same stage of breast cancer might have different factors that make up their stage.

Here are 3 examples of how all of the factors listed above are used to determine the pathologic (surgical) breast cancer stage:

Example #1

If the cancer size is between 2 and 5 cm (T2) but it has not spread to the nearby lymph nodes (N0) or to distant organs (M0) **AND** is:

- Grade 3
- HER2 negative
- ER positive
- PR positive

The cancer stage is IB.

Example #2

If the cancer is larger than 5 cm (T3) and has spread to 4 to 9 lymph nodes under the arm or to any internal mammary lymph nodes (N2) but not to distant organs (M0) **AND** is:

- Grade 2
- HER2 positive
- ER positive
- PR positive

The cancer stage is IB.

Example #3

If the cancer is larger than 5 cm (T3) and has spread to 4 to 9 lymph nodes under the arm or to any internal mammary lymph nodes (N2) but not to distant organs (M0) **AND** is:

- Grade 2
- HER2 negative
- ER negative
- PR negative

The cancer stage is IIIB.

These are only 3 examples out of many possible combinations of factors. To understand what your breast cancer stage is, and what it means, talk to your doctor.

Hyperlinks

- 1. www.cancer.org/cancer/types/breast-cancer/treatment.html
- 2. www.cancer.org/cancer/diagnosis-staging/staging.html

References

American Joint Committee on Cancer. Breast. In: AJCC Cancer Staging Manual. 8th ed. New York, NY: Springer; 2017:589.

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Survival Rates for Breast Cancer

Understanding the numbers

Survival rates can give you an idea of what percentage 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 of how likely it is that your treatment will be successful.

Keep in mind that survival rates are estimates and are often based on previous outcomes of large numbers of people who had a specific cancer, but they can't predict what will happen in any particular person's case. These statistics can be confusing and may lead you to have more questions. Talk with your doctor, who is familiar with your situation, about how these numbers may apply to you.

What is a 5-year relative survival rate?

A **relative survival rate** compares women with the same type and stage of breast cancer to women in the overall population. For example, if the **5-year relative survival rate** for a specific stage of breast cancer is 90%, it means that women who have that cancer are, on average, about 90% as likely as women who don't have that cancer to live for at least 5 years after being diagnosed.

Where do these numbers come from?

The American Cancer Society relies on information from the Surveillance,

Epidemiology, and End Results (SEER) database, maintained by the National Cancer Institute (NCI), to provide survival statistics for different types of cancer.

The SEER database tracks 5-year relative survival rates for breast cancer in the United States, based on how far the cancer has spread. The SEER database, however, does not group cancers by AJCC TNM stages (stage 1, stage 2, stage 3, etc.). Instead, it groups cancers into localized, regional, and distant stages:

- **Localized**: There is no sign that the cancer has spread outside of the breast.
- **Regional:** The cancer has spread outside the breast to nearby structures or lymph nodes.
- **Distant:** The cancer has spread to distant parts of the body such as the lungs, liver or bones.

5-year relative survival rates for breast cancer

These numbers are based on women diagnosed with breast cancer between 2012 and 2018.

SEER Stage	5-year Relative Survival Rate
Localized*	99%
Regional	86%
Distant	30%
All SEER stages combined	91%

^{*}Localized stage only includes invasive cancer. It does not include ductal carcinoma in situ (DCIS).

Understanding the numbers

- Women now being diagnosed with breast cancer may have a better outlook than these numbers show. Treatments improve over time, and these numbers are based on women who were diagnosed and treated at least five years earlier.
- These numbers apply only to the stage of the cancer when it is first diagnosed. They do not apply later on if the cancer grows, spreads, or comes back after treatment.

- These numbers don't take everything into account. Survival rates are grouped based on how far the cancer has spread, but your age, overall health, how well the cancer responds to treatment, tumor grade, the presence of hormone receptors on the cancer cells, HER2 status, and other factors can also affect your outlook.
- Survival rates for women with triple-negative breast cancer are different than those above. See <u>Triple-negative Breast Cancer</u>¹.
- Survival rates for women with inflammatory breast cancer are different than those above. See<u>Inflammatory Breast Cancer</u>².

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/triple-negative.html</u>
- 2. <u>www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/inflammatory-breast-cancer.html</u>

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Questions to Ask Your Doctor About Breast Cancer

- When you're told you have breast cancer
- When deciding on a treatment plan
- If you need surgery
- During treatment
- After treatment

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 clinical trials¹.

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-Doctor

When you're told you have breast cancer

- Exactly what type of breast cancer³ do I have?
- How big is the cancer? Where exactly is it?
- Has the cancer spread to my lymph nodes or other organs?
- What is the stage of my cancer? What does it 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?
- What is the grade 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 <u>genetic testing</u>⁴? What are my testing options? Should I take a home-based genetic test? What would be the reasons for and against testing?
- How do I get a copy of my pathology report?
- If I'm worried about the costs and <u>insurance coverage</u>⁵ 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 <u>second opinion</u>⁶? How do I do that? Will getting a second opinion delay my treatment and can that affect my outcome?
- What are my treatment choices?
- What treatment do you recommend and why?
- Should I think about taking part in a <u>clinical trial</u>⁸?
- 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?
- Should my biopsy tissue be sent for a gene expression test to help decide if chemotherapy might be helpful for me?
- Are there othermolecular or protein tests that need to be done on my cancer tissue to help decide my treatment options?
- 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?
- Do I have time to freeze my eggs before starting treatment? What are my options?
- 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 surgery9 (lumpectomy) an option for me? Why or why not?
- What are the positive and negative sides 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 surgery? Will I have normal feeling in them?
- What will the scar look like?
- Is <u>breast reconstruction surgery</u>¹⁰ 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 reasons for and against having it done right away or waiting until later?
- What types of reconstruction might be options for me?
- Could you recommend a plastic surgeon I could speak to 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 or concerns?

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 during treatment? If so, 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 <u>lymphedema</u>¹¹?
- 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?

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/finding-care/the-doctor-patient-relationship.html</u>
- 3. www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer.html
- 4. www.cancer.org/cancer/risk-prevention/genetics.html
- 5. <u>www.cancer.org/cancer/financial-insurance-matters/understanding-health-insurance.html</u>
- 6. www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html
- 7. www.cancer.org/cancer/types/breast-cancer/treatment.html

- 8. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 9. <u>www.cancer.org/cancer/types/breast-cancer/treatment/surgery-for-breast-cancer/breast-conserving-surgery-lumpectomy.html</u>
- 10. www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery.html
- 11. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html

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Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

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