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# **Understanding a Breast Cancer**

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><sup>1</sup> 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<sup>2</sup></u> for more on how DCIS is described.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-</u> 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

Finding out more information about the DNA in breast cancer cells can help predict how fast those cancer cells are dividing and growing. If you want to learn more about DNA and breast cancer, you should first understand two important terms: **ploidy** and **cell proliferation**.

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

If the S-phase fraction or Ki-67 labeling index is high, it means that the cancer cells are dividing more rapidly.

#### References

Duffy MJ, Harbeck N, Nap M, Molina R, Nicolini A, Senkus E, Cardoso F. Clinical use of biomarkers in breast cancer: Updated guidelines from the European Group on Tumor Markers (EGTM). *Eur J Cancer*. 2017;75:284-298.

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# **Breast Cancer Hormone Receptor Status**

Breast cancer cells taken out during a biopsy or surgery are tested to see if they have certain proteins that are **estrogen or progesterone receptors**. If your breast cancer cells have these receptors (proteins), this means that when the hormones estrogen and progesterone attach to the 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 of a cancer is important, because it helps determine the treatment options. Ask your cancer care team about your hormone receptor status and what it means for you.

- 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?

#### 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</u> <u>do this mean?B688 Tm 4p.37 Tm s151 72 3h43.y:drugs t,i receptorsWhat do the hormo ctuainmpo atr</u> 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><sup>2</sup> 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**

- 1. <u>www.cancer.org/cancer/types/breast-cancer/treatment/hormone-therapy-for-breast-cancer.html</u>
- 2. <u>www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/triple-negative.html</u>

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Allison KH, Hammond MEH, Dowsett M, et al. Estrogen and Progesterone Receptor Testing in Breast Cancer: ASCO/CAP Guideline Update. *J Clin Oncol.* 2020;38(12):1346-1366. doi:10.1200/JCO.19.02309.

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Goldberg J, Pastorello RG, Vallius T, et al. The Immunology of Hormone Receptor Positive Breast Cancer.

# **Breast Cancer HER2 Status**

**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<sup>2</sup></u> and <u>Understanding Your</u> <u>Pathology Report: Breast Cancer<sup>3</sup> to get more details about these tests.</u>

#### 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.

Often the IHC test for HER2 is done first. This is commonly followed by the FISH test to further classify the tumor type.

- If the IHC result is 0 with no membrane staining, the cancer is considered **HER2**-**negative**. These cancers do not respond to treatment with drugs that target HER2.
- If the IHC result is 0 with membrane staining (HER2+ staining in more than 0% but no more than 10% of tumor cells), the cancer is considered **HER2-ultralow**. These cancers may respond to certain drugs called antibody-drug conjugates.
- If the IHC is 1+ OR if the IHC is 2+ but FISH is negative, the cancer is considered **HER2-low**. These cancers may respond to certain drugs called antibody-drug conjugates.
- If the IHC is 2+ and the FISH is positive OR IHC is 3+, the cancer is **HER2**-**positive**. These cancers are usually treated with drugs that target HER2.

**Triple-negative** breast cancers 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><sup>4</sup> to learn more.

**Triple-positive** breast cancers 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. <u>www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests.html</u>
- 3. <u>www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-</u> <u>tests/understanding-your-pathology-report/breast-pathology/breast-cancer-</u> <u>pathology.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 Gene Expression Tests**

**Gene expression tests** are a form of <u>personalized medicine</u><sup>1</sup>. Personalized medicine is 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?
- Testing options

#### 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><sup>2</sup> after breast surgery (adjuvant chemotherapy.) <u>Hormone</u> <u>therapy</u><sup>3</sup> 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><sup>4</sup> 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)<sup>5</sup>.

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 lowrecurrence 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> <u>inhibitor</u><sup>6</sup>.
- 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>
- 4. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>
- 5. <u>www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/dcis.html</u>
- 6. <u>www.cancer.org/cancer/types/breast-cancer/treatment/hormone-therapy-for-breast-cancer.html</u>

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Krop I, Ismaila N, Andre F, et al. Use of Biomarkers to Guide Decisions on Adjuvant

# Other Breast Cancer Gene, Protein, and Blood Tests

This is sometimes called <u>precision or personalized medicine</u><sup>2</sup> 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
- Molecular tests for gene changes
- Blood tests

#### Tests for certain proteins on tumor cells

Lab tests might 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, molecular testing might be done to see how many copies of the *HER2* gene the cancer cells have. 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><sup>3</sup> 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><sup>4</sup> or c gene chanr3.42 Tm 0 0 0 rg /GSa. 0 g 1 0 0 1 72 28

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 changes that might be tested for include:

- BRCA1 and BRCA2 gene mutations: For women with an advanced HER2negative breast cancer, your doctor might test you (not your cancer cells) for a <u>hereditary BRCA1 or BRCA2 mutation</u><sup>5</sup> (gene change). If you have one of these gene changes, treatment with the targeted drugs, olaparib (Lynparza) or talazoparib (Talzenna) might be options.
- *PIK3CA, AKT1, and PTEN gene mutations:* These 3 genes code for proteins in the same signaling pathway inside cells that can help them grow. Cancer cells sometimes have changes in one of these genes. If you have advanced breast cancer that is hormone receptor-positive and HER2-negative, and if the cancer cells show changes in one of these genes, a targeted drug such as capivasertib (Truqap), alpelisib (Piqray), or inavolisib (Itovebi) might be an option, along with the hormone drug<sup>6</sup> fulvestrant (and possibly other medicines).
- **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 (Jemperligs ( )Tj 0 g /F2 12 Tf 0 0 0 rg 00 0 0 rg /GS869 gs (ge10 0 r

• *NTRK* gene changes: 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 (Burtast cancer.

detection/breast-biopsy.html

- 2. www.cancer.org/cancer/managing-cancer/treatment-types/precision-medicine.html
- 3. www.cancer.org/cancer/types/breast-cancer/treatment/immunotherapy.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/risk-and-prevention/genetic-testing.html</u>
- 6. <u>www.cancer.org/cancer/types/breast-cancer/treatment/hormone-therapy-for-breast-cancer.html</u>

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# Imaging Tests to Look for Breast Cancer Spread

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

## Chest x-ray

A <u>chest x-ray<sup>1</sup></u> may be done to see if the cancer has spread to your lungs.

# Computed tomography (CT) scan

A <u>CT scan</u><sup>2</sup> 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, <u>MRI scans</u><sup>3</sup> 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><sup>4</sup> (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<sup>5</sup></u>

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

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><sup>1</sup> it. Doctors also use a cancer's stage when talking about <u>survival</u> statistics.

- What are the breast cancer stages?
- How is the stage determined?
- Details of the TNM staging system
- Examples using the full staging system

# What are the breast cancer stages?

The earliest stage breast cancers are

• 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 <u>Cancer Staging</u><sup>2</sup>.

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

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.

**MO:** 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.

# Hyperlinksarm or to any/3 0 0 0 rg /GS17\_em Ts 0 g c0Tj ET BT 1 0 0r to an5.5 IB.

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.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Breast Cancer. Version 8.2021. Accessed at https://www.nccn.org/professionals/physician\_gls/pdf/breast.pdf on September 15, 2021.

Paik, S. Development and Clinical Utility of a 21-Gene Recurrence Score Prognostic Assay in Patients with Early Breast Cancer Treated with Tamoxifen. *The Oncologist.* 2007;12(6): 631-635.

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# **Survival Rates for Breast Cancer**

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?
- Where do these numbers come from?

- 5-year relative survival rates for breast cancer
- Understanding the numbers

# What is a 5-year relative survival rate?

A relative survival rate compares women with the same type and stage of breast

Distant	32%
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 from those above. See <u>Triple-negative Breast Cancer</u><sup>1</sup>.
- Survival rates for women with inflammatory breast cancer are different from those above. See<u>Inflammatory Breast Cancer</u><sup>2</sup>.

# 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>

#### References

American Cancer Society. *Cancer Facts & Figures 2025.* Atlanta: American Cancer Society; 2025.

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# **Questions to Ask Your Doctor About Breast Cancer**

(prognosis)?

- What are my chances of survival, based on my cancer as you see it?
- Should I think about <u>genetic testing</u><sup>2</sup>? 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><sup>3</sup> 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><sup>4</sup>? How do I do that? Will getting a second opinion delay my treatment and can that affect my outcome?
- What are my treatment<sup>5</sup> choices?
- What treatment do you recommend and why?
- Should I think about taking part in a <u>clinical trial</u><sup>6</sup>?
- 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 <u>breast-conserving surgery</u><sup>7</sup> (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><sup>8</sup> 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<sup>9</sup>?</u>
- 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?

# Preparing your list of questions

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 <u>The Doctor-Patient</u> <u>Relationship</u><sup>11</sup>.

# **Hyperlinks**

- 1. www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer.html
- 2. <u>www.cancer.org/cancer/risk-prevention/genetics.html</u> <u>www.cancer.org/cancer/financial-insurance-matters/understanding-health-</u> <u>insurance5 w 72 632.02 m 138.02 632can9/types-of-brrrrrrrrrrrrrrrrrrrr10/Tj ET8 0.rr4n()Tj745 RG 0.75</u>