Pathology Report

The **pathology report** is a detailed description of your cancer at the time of surgery. It provides information unique to your cancer — where the tumor was located, how big it was, what kind of cells it contained, characteristics of the cancer and whether it has spread into surrounding tissues of the duct or lobule in which it began. These vital pieces of information are crucial for the next step — planning your treatment.

A pathology report starts when an abnormal or suspicious area is removed from your breast for microscopic examination. The tissue is then sent to a pathology laboratory where a pathologist (a physician who specializes in diagnosing disease from tissue specimens) analyzes it and prepares a pathology report. The analysis reveals whether the tissue is benign (noncancerous) or malignant (cancerous) and helps the surgeon determine if additional surgery is needed. If a malignancy is diagnosed, the pathology report provides physicians with the information needed to develop a treatment plan based on the findings.

Because of the importance of the pathology analysis, many controls and guidelines are in place to promote accuracy. When the physician removes the specimen, it is placed in a container with your name, hospital number, date and specimen identification number. The surgeon or radiologist who performed the biopsy also includes specific details about the specimen. In the lab, the pathologist writes a report on what can be visually seen without the use of any special devices, procedures or chemicals. This may include a description of the specimen color, size of the specimen (not size of cancer), any marking or inking of margins done by the surgeon, weight, type of biopsy or surgical procedure performed (lumpectomy or mastectomy) and the presence of lymph nodes, if removed. The pathologist then cuts or sections the lump to be viewed under the microscope. The tissue may be prepared for examination by either frozen section or permanent section.

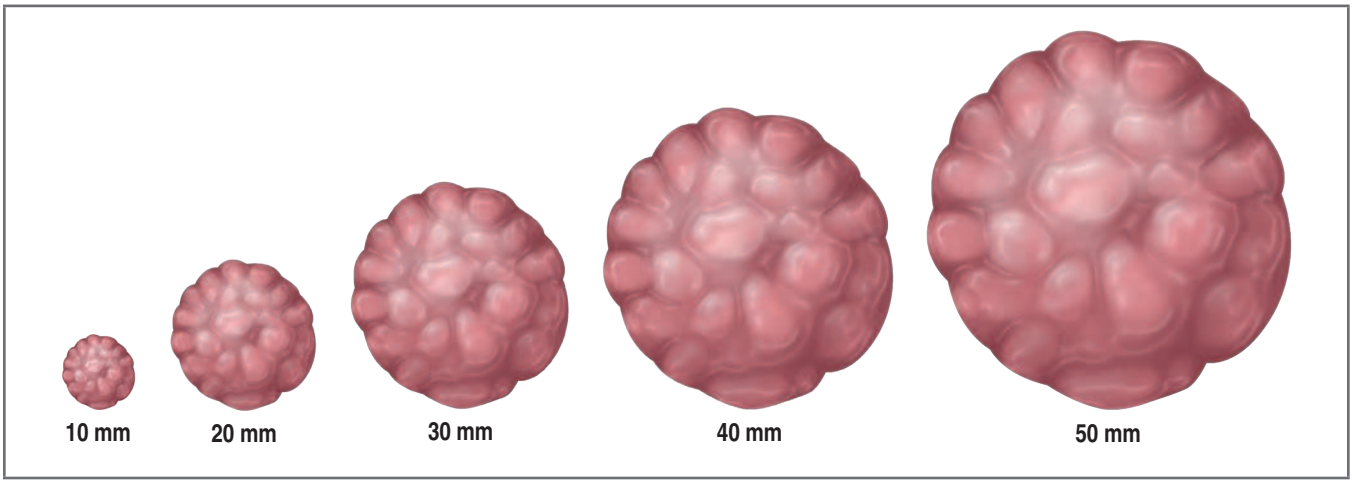
A frozen section is a quick analysis of the tissue, most commonly used during sentinel lymph node surgery. A frozen section is prepared while the patient is still under anesthesia to allow the surgeon to know if additional nodes need to be removed while the patient is still in surgery. A frozen section is prepared within minutes after the specimen arrives at the laboratory. The pathologist quickly freezes the tissue by applying a chemical to instantly harden or “fix” the biopsy. The pathologist can review this tissue and offer an opinion in a few minutes as to whether it is benign or malignant. Frozen section analysis is usually as accurate as a permanent section, but the pathologist only views a small portion of the tumor. The problem occurs when there are no cancer cells present. The diagnosis cannot be definitive until all the tissues are carefully examined. Thus, the results of the permanent section are more comprehensive.

A permanent section is prepared by placing the remaining specimen in a chemical (formalin) solution that fixes the tissue, similar to boiling an egg. When the permanent section is firm, in approximately 24 hours, the tissue is cut into small sheets (thinner than tissue paper), and mounted on glass slides. The pathologist then views the slides under a microscope and issues a report on what is seen. The slides are carefully stored so that they may be reviewed in the future, if necessary. A permanent section gives the most comprehensive answer because the pathologist studies all the tissues removed by the surgeon.

What Does the Pathologist Look For?

In reviewing the tissue, the pathologist prepares a pathology report to give information on different aspects of the tumor. During your diagnosis for breast cancer you will have two pathology reports, one after your biopsy and another after your surgery. The biopsy pathology report will not contain as much information as your final pathology report. Biopsy pathology reports are a guide to determine if you need to have breast cancer surgery. The final pathology report is used by your physician to determine the type of treatment for your cancer. Information in pathology reports will vary according to the type of specimen tested.

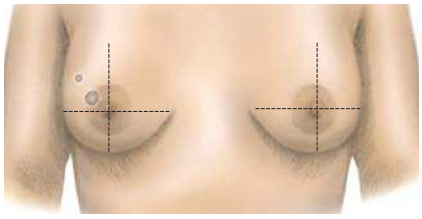
- **Tumor Size** — Measures size of tumor; largest dimension is reported in centimeters or millimeters (10 mm equals 1 cm; 1 cm equals ⅜ inch; 1 inch equals 2.5 cm).



- **Tumor Focus** — States the number of sites in which cancer is found. Most often, only one site of cancer is found.
  - **Cancer May Be Found As:**
    - A single tumor in the specimen
    - More than one tumor in the specimen
    - A tumor, or tumors, along with in situ cancer in the specimen

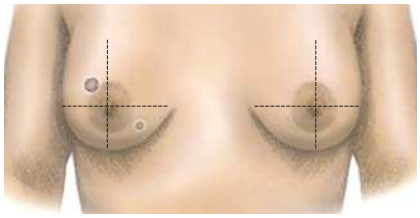
  The term **multifocal** means two abnormalities are found within one quadrant (¼) area of the breast. The term **multicentric** means that the abnormalities are located in more than one quadrant of the breast.
- **Extent of Tumor** — Reports if the tumor has extended to involve the breast skin, nipple or muscle of the chest wall.

Multifocal



Additional Cancer Found in the Same Quadrant of the Breast

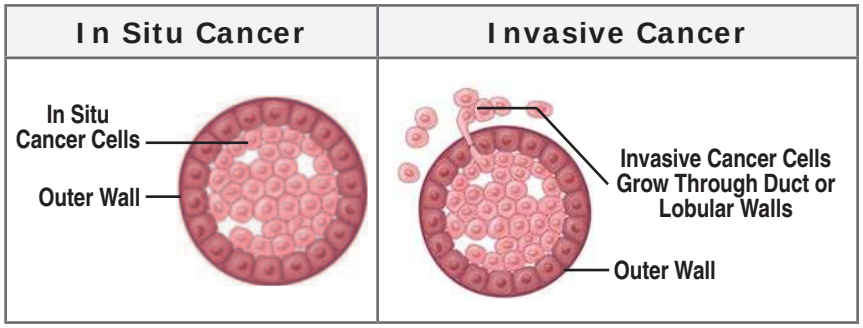
Multicentric



Additional Cancer Found in Different Quadrants of the Breast

Tumor Invasiveness:

- **In Situ Cancer** — Normal ducts and lobules are lined with one or two layers of cells that are in an orderly pattern. When in situ cancer develops and grows, it does not break through the walls but remains in the duct or lobule where it began. This type of cancer has a good prognosis.

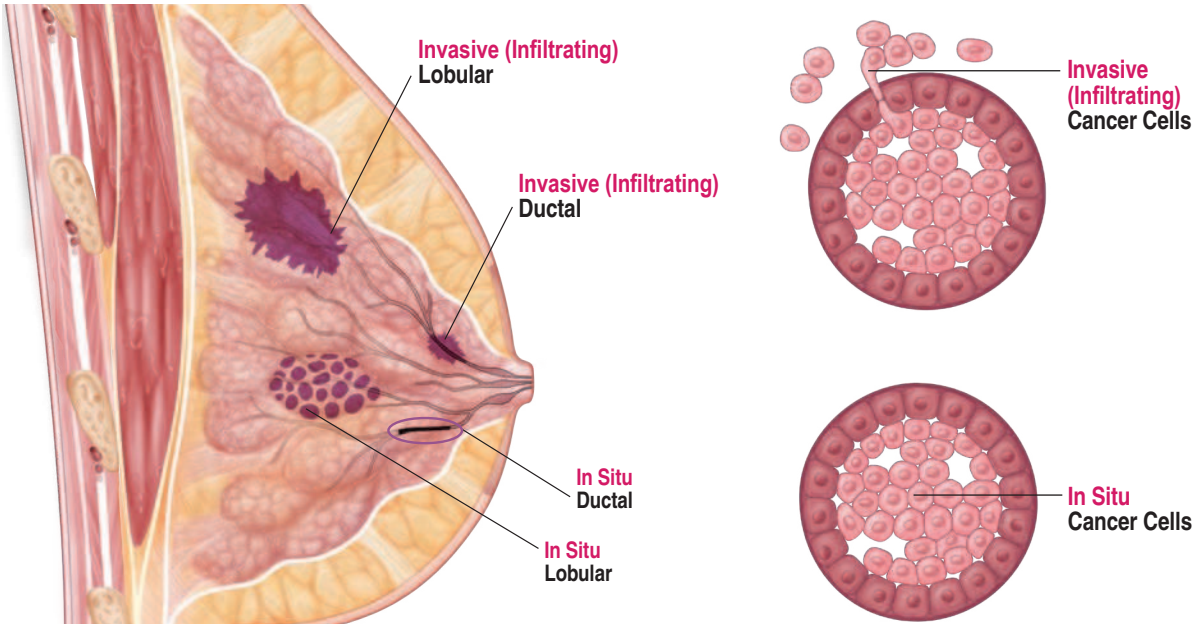


- **Invasive Cancer** — Indicates that the cancer has broken through the wall of the duct or lobule and has begun to grow into the surrounding tissue becoming invasive. "Microinvasive" means that just a small amount of cells have grown through the cell walls.

Major Types of Cancer:

- **Ductal Carcinomas** — The majority of breast cancers are identified as ductal carcinomas meaning the cancer was found to originate in the ducts of the breast. Ductal carcinomas may be in situ (ductal carcinoma in situ, DCIS) or invasive (invasive ductal carcinoma).
- **Lobular Carcinomas** — Lobular carcinomas start in the lobules of the breast gland, the fluid producing part of the breast. They may also be in situ (lobular carcinoma in situ, LCIS) or invasive (invasive lobular carcinoma).

Ductal & Lobular Carcinomas



Grading of In Situ Cancers

Lobular carcinoma in situ cancer (LCIS) is noted in a pathology report but not graded. Ductal carcinoma in situ (DCIS) is graded according to:

- **Pattern** — Refers to the growth pattern of the cells in the duct. Types include solid, cribriform, micropapillary, papillary and comedo.
- **Grade** — Refers to the degree of abnormality in the cells and nuclei.
  - **Grade 1 (low)** — the cells are small and uniform
  - **Grade 2 (intermediate)** — the cells have features between low and high grade
  - **Grade 3 (high)** — the cells have a disorganized growth pattern, increased size, variation in size and abnormal nuclei
- **Estimated Size (Extent) of DCIS** — The ducts in the breast are like the stems of a bunch of grapes. DCIS grows along the "stems" or ducts so the DCIS may extend over a large area. The pathologist will give a measurement of the estimated size of the DCIS (in millimeters).
- **Margin Evaluation** — The cut edges of the surgical biopsy specimen are called the margins. Pathologists examine the margins to determine how the cancer cells relate to the margin. Surgical margins are described as: **negative** (none found), **positive** (involved), **close to a margin** or **indeterminate** (could not specify). (See explanation on page 5).
- **Necrosis** — Refers to dead tumor cells in the DCIS. Necrosis is frequently seen in the higher grades of DCIS.

Van Nuys Prognostic Index (Used to Grade DCIS)

1. Nuclear Grade — **Grade Value** Non-high grade without necrosis ..... 1 point Non-high grade with necrosis ..... 2 points High grade with necrosis ..... 3 points	Evaluates size and shape of nucleus of cells
2. Tumor Size — **Grade Value** 15 mm and under (< 1.5 cm) ..... 1 point 16 mm to 40 mm (1.6 - 4.0 cm) ..... 2 points 41 mm or greater (> 4.1 cm) ..... 3 points	Evaluates size of the area where DCIS is found
3. Tumor Margins — **Grade Value** 10 mm or greater (> 1 cm) ..... 1 point 1 - 9 mm (0.1 - < .9 cm) ..... 2 points 1 mm or under (<.1 cm) ..... 3 points	Evaluates distance from DCIS to margins of surgical specimen
4. Age at Diagnosis — **Age Value** Over 60 ..... 1 point 40 - 60 ..... 2 points Under 40 ..... 3 points	Factors in age at diagnosis
Final Cumulative Total **4 - 6 points** = no difference in survival-free local recurrence lumpectomy with/without radiation therapy **7 - 9 points** = significant decrease in local recurrence with radiation therapy **10 - 12 points** = high rate of local recurrence, mastectomy recommended	**Total of the scores in the above four areas determines final grade**

Histological Grading of Invasive Cancers

Some pathologists use the Nottingham combined histologic grade for grading invasive tumors. This grading system gives a number from 1 to 3 according to aggressiveness of three different characteristics of the tumor: (1) tubule formation, (2) nuclear size and shape and (3) mitotic count (how fast the cells are growing). The grade values from each characteristic are then added together to provide a final cumulative total. A combined score of 3 – 5 points is designated as grade 1 (least aggressive); a combined score of 6 – 7 is grade 2; a combined score of 8 – 9 is grade 3 (most aggressive).

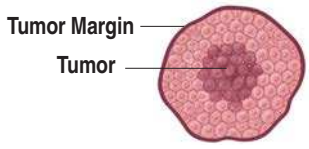
Nottingham Combined Histologic Grade
(Elston-Ellis Modification of Scarff-Bloom-Richardson Grading System)

1. Tubular Formation — **Grade Value** Majority (Over 75%) ..... 1 point Moderate degree (10 to 75%)..... 2 points Little or none (Under – 10%)..... 3 points	Evaluates cell arrangement for characteristics of looking like a small tube
2. Nuclear Shape/ Size — **Grade Value** Uniform, small nuclear shapes..... 1 point Moderate increase in size and varying shapes..... 2 points Marked abnormalities (often large nucleus) ..... 3 points	Evaluates size and shape variation of cells and nucleus of cells
3. Cell Division Rate — **Grade Value** Low (0 – 9)..... 1 point Moderate degree (10 – 19)..... 2 points High (Over 20) ..... 3 points	Determines how many cells are visible in the dividing stage in an area of the tumor
Final Cumulative Total — **Points** Grade 1 – Low-grade tumor ..... 3 – 5 points Grade 2 – Intermediate-grade tumor ..... 6 – 7 points Grade 3 – High-grade tumor..... 8 – 9 points	Total of the scores in the above three areas of evaluation determines final grade

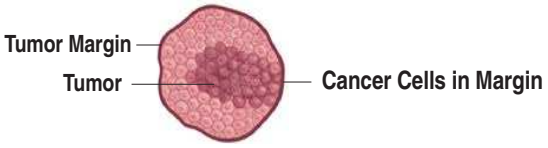
- **Margins** — Describes the area of tissue surrounding a tumor, if the entire tumor was removed during a lumpectomy or mastectomy, and how the margins relate to the tumor. When clear margins are not obtained the potential for local disease recurrence is increased and the treatment plan will take this into consideration. Terms to describe pathology margins:
  - **Negative, Clear, Clean or Uninvolved:** No evidence of cancer cells in the margins.
  - **Positive, Involved or Residual Cancer:** Cancer was found in the margins.
  - **Close:** Cancer cells are close to margins.
  - **Indeterminate:** Pathologist could not determine margin status.

Margins

Negative, Clear, Clean or Uninvolved:



Positive, Involved or Residual Cancer:



- **Lymph Node Status** — If surgery involved lymph node removal, the method of surgical removal (sentinel node using radiotracer/dye or axillary dissection) will be stated on the report. The area from which the node(s) was removed, along with the number of nodes sent to pathology will also be reported. The report will also describe the largest size of any cancer found in the lymph node(s) and whether the cancer invades tissue outside the node(s).
  - **Results of node evaluation will be reported as:**
    - **Lymph Node Negative** — Means that no cancer was found in the nodes.
    - **Lymph Node Positive** — Means that cancer was found in the nodes. The number of nodes with cancer will be stated in the report.
- **Pathological Staging** — A final staging of the cancer will be reported as TN (tumor/node) on a pathology report. This is based on the size of the tumor, the clinical features, chest wall involvement and lymph node involvement. The physician will determine through additional diagnostic tests if there is distant metastasis. The staging will then be TNM (tumor/node/metastasis). The M staging is not available in the pathology report. This information will come from your physician. The staging system most commonly used for breast cancers is the American Joint Committee on Cancer (AJCC) staging system. This system utilizes (T) the extent of the primary tumor, (N) the absence or presence of cancer in the lymph nodes and (M) the existence of metastasis, which will be provided by your physician.

American Joint Committee on Cancer (AJCC) Staging System

AJCC staging provides more specific details about your tumor, nodes and distant staging by adding information after the T, N and M. This information about your tumor provides a complete explanation of the characteristics of your tumor.

T (Tumor) Stages

- **TX:** Primary tumor cannot be assessed
- **T0:** No evidence of tumor a primary tumor
- **Tis (DCIS):** Ductal carcinoma in situ
- **Tis (Paget):** Paget Disease not associated with invasive carcinoma and/or carcinoma in situ
- **T1:** Tumor 20 mm or less in greatest dimension
- **T2:** Tumor more than 20 mm but not more than 50 mm in greatest dimension
- **T3:** Tumor more than 50 mm in greatest dimension
- **T4:** Tumor of any size with direct extension to the chest wall and/or to the skin

N (Node) Stages

- **NX:** Regional lymph nodes cannot be assessed
- **N0:** No regional lymph node involvement
- **N0(i+):** Isolated tumor cell clusters
- **N1mi:** Micrometastasis
- **N1 - N3:** Involvement of regional lymph nodes (number or extent of spread)

M (Metastases) Stages

M staging will be completed by your physician using different tests and scans to detect cancer outside of the breast area. Your physician will tell you in additional cancer is found.

- **MX:** Distant spread cannot be detected
- **M0:** No evidence of distant metastasis (cancer has not spread)
- **M0(i+):** Microscopic evidence of tumor cells in the blood, bone marrow or lymph nodes
- **M1:** Distant metastasis (cancer has spread to distant parts of the body)

Prognostic Tests

There are many diagnostic tests being used to evaluate tumors. Each of these tests collects pieces of the puzzle needed for your physician to determine your treatment plan.

- **Cell Proliferation Rate:** Determines the cancer cells' growth rate and can be evaluated during pathology by:
  - **S-phase Fraction Test:** Identifies the number of cells in the "synthesis phase" (the period right before a cell divides). Counts below 6 percent are considered low; counts of 6 to 10 percent are considered intermediate; counts over 10 percent are consider high.
  - **Ki-67:** A proliferation study that measures a protein in a cell that increases prior to dividing. Study results below 10 percent are considered low; counts of 10 to 20 percent are considered borderline; counts over 20 percent are considered high.
- **Hormone Receptor Assay** — Hormone receptor assay is a test that measures the presence of estrogen (ER) and progesterone (PR) receptors in the tumor cell nuclei and is performed on all invasive breast cancers. It tells the physician whether the tumor was stimulated to grow by female hormones and is very important in determining what type of treatment will be used after surgery. If a tumor is positive, that means it was stimulated by estrogen or progesterone and usually carries a more positive prognosis.
  - **Tumors May Be:**
    - » ER positive (+) PR positive (+)
    - » ER positive (+) PR negative (-)
    - » ER negative (-) PR positive (+)
    - » ER negative (-) PR negative (-)
- **HER2/ neu** — A gene that is over-expressed or amplified in about 25 to 30 percent of breast cancers. HER2/neu is evaluated in all invasive breast cancer specimens. Elevation of HER2 indicates a more aggressive cancer. However, identification of elevation indicates that a drug called Herceptin® which targets the HER2/neu receptor is an appropriate treatment choice.
- **Blood Vessel or Lymphatic Invasion** — A microscopic examination of the tumor will show if the surrounding blood vessels (vascular) or lymphatic vessels have been invaded by the tumor. No invasion offers a better prognosis.
- **Multigene Testing:** Tests are usually ordered from an outside lab (Oncotype DX®, MammaPrint®, Prosigna®, EndoPredict®, Breast Cancer Index®, Mammostrat® or IHC4®) for Stage 1 or Stage 2 cancers. The two most common genes associated with increased risk for breast cancer are BRCA1 and BRCA2 mutations. Other gene mutations have also been identified that may increase a patient's risk. Multigene testing may include 12 – 70 of these gene mutations. Common genes tested in multigene testing include: ATM, BARD, CDH1, CHEK2, NBN, NF1, PALB2, PTEN and STK11.

Triple Negative Breast Cancer

The term "triple negative" breast cancer describes a woman's cancer when tests for three different breast cancer receptors are all negative. A triple negative breast cancer is one that is (1) negative for estrogen receptors (ER), (2) negative for progesterone receptors (PR) and (3) negative for HER2 receptors (human epidermal growth factor receptor 2). Many drugs used in cancer treatment are designed to target one of these positive receptor sites, thus a triple negative breast cancer diagnosis limits the use of some medications. Triple negative women, however, are typically responsive to chemotherapy drugs that are not targeted at ER/PR or HER2 receptor sites.

Pathology Report

The pathologist prepares a written report that is sent to your physician. If the hospital or cancer center conducts multidisciplinary conferences, the pathologist presents the findings at the conference. Time varies as to when the final report will be available. Many pathologists have a commitment to report within 24 hours after receiving the specimen. Ask your physician when you can expect to receive your pathology report. If the diagnosis reveals cancer, the pathologist's findings will help the physician(s) determine what further treatments will be needed. Additional diagnostic tests, such as a bone scan, liver scan, chest X-ray, CT scan or an MRI (magnetic resonance imaging), may be ordered. When all the results are received from the tests, your cancer

will be staged on a scale from zero (in situ cancer) to four (a cancer with distant metastasis). A stage zero cancer is the least aggressive and has the best prognosis.

Pathology Report Summary

The bottom-line information is contained in the summary or final diagnosis section of your pathology report. Combining information from all of the other sections of the pathology report will provide a synopsis of the most important information regarding your cancer.

Pathology Report Questions

When you discuss the findings of your pathology report with your physician, you may want to ask the following questions and write down the answers. Some doctors will provide a copy of your pathology report for your records.

- What is the name of the type of cancer I have?
- Was my tumor in situ (inside ducts or lobules) or invasive (grown through the walls of the ducts or lobules)?
- What size was my tumor? (The size is in millimeters (mm) or centimeters (cm). 10 mm equals 1 cm. 1 cm equals 3/8 inch. 1 inch equals approximately 2.5 cm.)
- Was the cancer found anywhere else in my breast tissue?
- How many lymph nodes were removed? How many levels of lymph nodes did you sample or remove? (You have three levels of nodes.)
- Were any nodes positive with cancer cells?
- Was my tumor estrogen or progesterone receptor positive?
- Was my tumor HER2/neu positive?
- Did you grade my tumor on a grading scale and if so, what was the final cumulative score? (Grade 1: least aggressive; Grade 3: most aggressive)
- Is there anything else that I need to know about my cancer?

After the Pathology Report

Obviously, you have no control over the findings described in your pathology report. However, you can become an active participant with your physicians to help defeat the disease.

Remember:

- Breast cancer is a treatable disease. It certainly is not an illness you would choose, but it is an illness with many proven treatments.
- Acquire an understanding of the treatment options. This will allow you to communicate with your healthcare team and become an active participant in decisions. Understanding will alleviate many irrational fears and restore a sense of control to your life.

Employ the best of all medicines—your attitude. The most productive approach you can bring, and one which the physician cannot provide, is a positive, cooperative attitude. Determination, combined with optimism, creates a healing environment that only you can provide.

Additional Information:

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