PROGNOSTIC MARKERS

***Quick Summary* of Section**

Margins or ink	• When an entire tumor is removed, the outside edges (or margins) of the specimen are coated with ink, sometimes even with different colors of ink on different sides of the specimen.
HER2/neu gene	• Some breast cancers have too much of a growth-promoting protein called HER2/neu (HER2). The HER2/neu gene instructs the cells to make this protein. • *Immunohistochemistry (IHC)* • *Fluorescent in situ hybridization (FISH*) • *Chromogenic in situ hybridization (CISH)*
Estrogen receptor (ER)	• Estrogen receptor (ER): A protein found inside the cells of the female reproductive tissue, some other types of tissue, and some cancer cells. The hormone estrogen will bind to the receptors inside the cells and may cause the cells to grow.
Progesterone receptor (PR)	• Progesterone receptor (PR): A protein found inside the cells of the female reproductive tissue, some other types of tissue, and some cancer cells. The hormone progesterone will bind to the receptors inside the cells and may cause the cells to grow.
Ki-67	• Ki-67 is a way to measure how fast the cancer cells are growing and dividing.
S-phase fraction	• This number tells you what percentages of cells in the sample are in the process of copying their genetic information, or DNA.
Lymphovascular Invasion	• Lymphovascular invasion (LVI) is defined as the presence of tumor cells within a definite endothelial-lined space (lymphatics or blood vessels) in the breast surrounding invasive carcinoma.
Multigene tests	• Tests in which samples of tissue are studied to look at the activity of many genes at the same time. These tests may help predict whether cancer will spread to other parts of the body or recur (come back).
Molecular subtypes	• Four main breast cancer subtypes have been identified according to estrogen receptor (ER), progesterone receptor (PR), and HER2. *These subtypes include luminal types A and B, basal-like, and HER2-enriched subtype.*

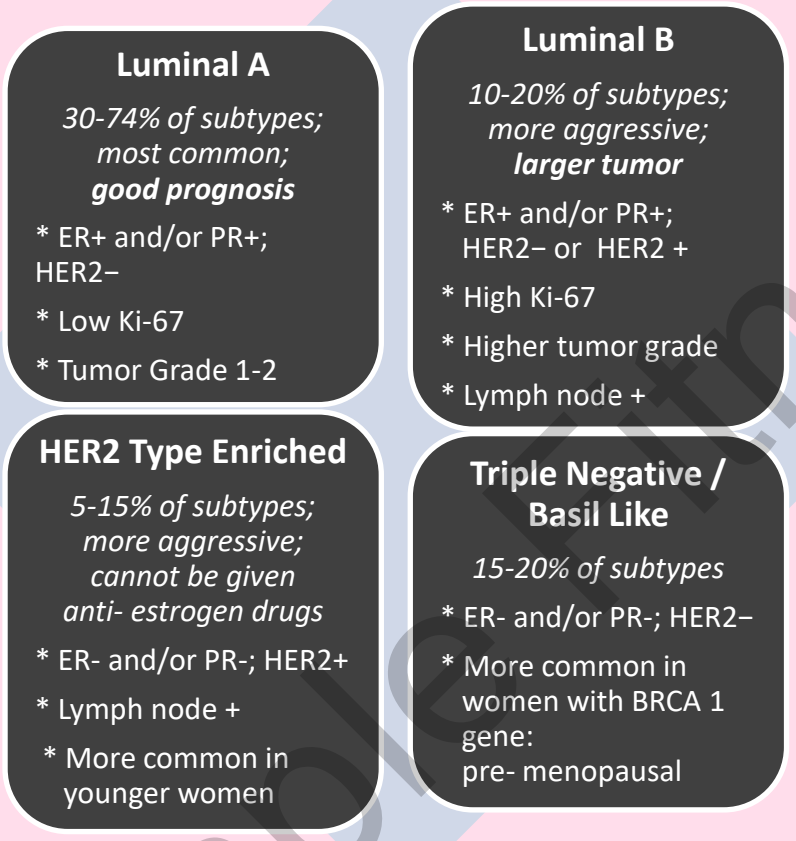
Margins or Ink	When an entire tumor is removed, the outside edges (or margins) of the specimen are coated with ink, sometimes even with different colors of ink on different sides of the specimen. • The pathologist looks at slides of the tumor under the microscope to see how close the cancer cells get to the ink (the edges or margins of the specimen). *American Cancer Society: Understanding Your Pathology Report* • The margin is described as negative or clean when the pathologist finds no cancer cells at the edge of the tissue, suggesting that all of the cancer has been removed. • The margin is described as positive or involved when the pathologist finds cancer cells at the edge of the tissue, suggesting that all of the cancer has not been removed. *NIH – NCI (1)*
HER2/neu gene *IHC and FISH test*	Some breast cancers have too much of a growth-promoting protein called HER2/neu (HER2). The HER2/neu gene instructs the cells to make this protein. • Tumors with increased levels of HER2/neu are referred to as HER2-positive. • The cells in HER2-positive breast cancers have too many copies of the HER2/neu gene, resulting in greater than normal amounts of the HER2 protein. These cancers tend to grow and spread more quickly than other breast cancers. • Women with HER2-positive cancers are much more likely to benefit from treatment with drugs that target the HER2 protein. If your cancer is HER2-positive, your doctor might add certain drugs to your treatment. How the results of your tests will affect your treatment is best discussed with your doctor. Testing of the biopsy or surgery sample: ***Immunohistochemistry (IHC):*** In this test, special antibodies that will stick to the HER2 protein are applied to the sample, which cause cells to change color if many copies are present. This color change can be seen under a microscope. The test results are reported as 0, 1+, 2+, or 3+. • **0 or 1+: HER2- (negative).** Women with HER2- negative tumors are not treated with drugs that target HER2. • **3+ : HER2 + (positive).** The person might benefit from treatment with drugs that target HER2. • **2+: 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. ***Fluorescent in situ hybridization (FISH*)**: This test uses fluorescent pieces of DNA that specifically stick to copies of the HER2/neu gene in cells, which can then be counted under a special microscope. ***Chromogenic in situ hybridization (CISH)*:** This test works similarly to FISH, by using small DNA probes to count the number of HER2/neu genes in breast cancer cells. *American Cancer Society: Understanding Your Pathology Report*

Estrogen receptor (ER)	Estrogen: A type of hormone made by the body that helps develop and maintain female sex characteristics and the growth of long bones. Estrogens can also be made in the laboratory. They may be used as a type of birth control and to treat symptoms of menopause, menstrual disorders, osteoporosis, and other conditions. • **Estrogen receptor (ER):** A protein found inside the cells of the female reproductive tissue, some other types of tissue, and some cancer cells. The hormone estrogen will bind to the receptors inside the cells and may cause the cells to grow. Also called ER. • **Estrogen receptor negative (ER-):** Describes cells that do not have a protein to which the hormone estrogen will bind. Cancer cells that are estrogen receptor negative do not need estrogen to grow, and usually do not stop growing when treated with hormones that block estrogen from binding. Also called ER negative. • **Estrogen receptor positive (ER+):** Describes cells that have a receptor protein that binds the hormone estrogen. Cancer cells that are estrogen receptor positive may need estrogen to grow, and may stop growing or die when treated with substances that block the binding and actions of estrogen. Also called ER positive. • **Estrogen receptor (ER) test**: A lab test to find out if cancer cells have estrogen receptors (proteins to which estrogen will bind). If the cells have estrogen receptors, they may need estrogen to grow, and this may affect how the cancer is treated. *NIH – NCI (2)* Results for ER are reported separately and can be reported in different ways: • Negative, weakly positive, positive • Percent positive • Percent positive and whether the staining is weak, moderate, or strong. *Women with hormone receptor-positive cancers tend to have a better prognosis and are much more likely to respond to hormone therapy than women with cancers without these receptors.* *American Cancer Society: Understanding Your Pathology Report*

Progesterone receptor (PR)	Progesterone: A type of hormone made by the body that plays a role in the menstrual cycle and pregnancy. Progesterone can also be made in the laboratory. It may be used as a type of birth control and to treat menstrual disorders, infertility, symptoms of menopause, and other conditions. • **Progesterone receptor (PR):** A protein found inside the cells of the female reproductive tissue, some other types of tissue, and some cancer cells. The hormone progesterone will bind to the receptors inside the cells and may cause the cells to grow. Also called PR. • **Progesterone receptor negative (PR-):** Describes cells that do not have a protein to which the hormone progesterone will bind. Cancer cells that are progesterone receptor negative do not need progesterone to grow, and usually do not stop growing when treated with hormones that block progesterone from binding. Also called PR negative. • **Progesterone receptor positive (PR+):** Describes cells that have a protein to which the hormone progesterone will bind. Cancer cells that are progesterone receptor positive need progesterone to grow and will usually stop growing when treated with hormones that block progesterone from binding. Also called PR positive. • **Progesterone receptor (PR) test:** A lab test to find out if cancer cells have progesterone receptors (proteins to which the hormone progesterone will bind). If the cells have progesterone receptors, they may need progesterone to grow, and this can affect how the cancer is treated. *NIH – NCI (3)* Results for PR are reported separately and can be reported in different ways: • Negative, weakly positive, positive • Percent positive • Percent positive and whether the staining is weak, moderate, or strong. *Women with hormone receptor-positive cancers tend to have a better prognosis and are much more likely to respond to hormone therapy than women with cancers without these receptors.* *American Cancer Society: Understanding Your Pathology Report*
Ki-67	Ki-67 is a way to measure how fast the cancer cells are growing and dividing. • High values (over 30%) for Ki-67 mean that many cells are dividing, so the cancer is likely to grow and spread more quickly". *American Cancer Society: Understanding Your Pathology Report* • Less than 10% - low • 10-20/25% - borderline, • More than 20-25% - high The higher the percentage, the more aggressive the cancer is. *BreastCancer.org: Rate of Cell Growth*
S-phase fraction	This number tells you what percentages of cells in the sample are in the process of copying their genetic information, or DNA. This S-phase, short for "synthesis phase," happens just before a cell divides into two new cells. *BreastCancer.org: Rate of Cell Growth* • Less than 6% - low • 6-10% - intermediate • More than 10% - high.

Lymphovascular Invasion	Lymphovascular invasion (LVI) is defined as the presence of tumor cells within a definite endothelial-lined space (lymphatics or blood vessels) in the breast surrounding invasive carcinoma. • The presence of LVI is associated with an increased risk of axillary lymph node and distant metastases. • Although the mechanism of LVI has not been completely elucidated, LVI is considered as a prognostic factor in patients with operable breast cancer with or without metastatic axillary lymph nodes who are undergoing adjuvant treatment. *NCBI – PMC Lymphovascular invasion*
Multigene tests	Tests in which samples of tissue are studied to look at the activity of many genes at the same time. These tests may help predict whether cancer will spread to other parts of the body or recur (come back). There are many types of multigene tests. The following multigene tests have been studied in clinical trials: • **Oncotype DX**: This test helps predict whether early-stage breast cancer that is estrogen receptor positive and node negative will spread to other parts of the body. If the risk that the cancer will spread is high, chemotherapy may be given to lower the risk. • **MammaPrint**: A laboratory test in which the activity of 70 different genes is looked at in the breast cancer tissue of women who have early-stage invasive breast cancer that has not spread to lymph nodes or has spread to 3 or fewer lymph nodes. The activity level of these genes helps predict whether breast cancer will spread to other parts of the body or come back. If the test shows that the risk that the cancer will spread or come back is high, chemotherapy may be given to lower the risk. *NIH – NCI (2*)

Molecular subtypes	Four main breast cancer subtypes have been identified according to estrogen receptor (ER), progesterone receptor (PR), and HER2. These subtypes include luminal types A and B, basal-like, and HER2-enriched subtype.



NCBI – NIH (1) and Klose Training: Breast Cancer Rehab

American Cancer Society: Understanding Your Pathology Report: Breast Cancer *https://www.cancer.org/treatment/understanding-your-diagnosis/tests/understanding-your-pathology-report/breast-pathology/breast-cancer-pathology.html*

BreastCancer.org: Rate of Cell Growth *https://www.breastcancer.org/symptoms/diagnosis/rate_grade*

Klose Training: Breast Cancer Rehab Course *https://klosetraining.com/*

NCBI – NIH Ki-67 as a prognostic marker *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5250608/*

NCBI – PMC Lymphovascular invasion *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6078671/*

NIH – NCI (1) - Breast Treatment (professional) *https://www.cancer.gov/types/breast/hp/breast-treatment-pdq*

NIH – NCI (2) Treatment (patient) *https://www.cancer.gov/types/breast/patient/breast-treatment-pdq#_181*

NIH – NCI (5) Tumor Grade *https://www.cancer.gov/about-cancer/diagnosis-staging/prognosis/tumor-grade-fact-sheet*

NIH – NCI (6) Staging *https://www.cancer.gov/about-cancer/diagnosis-staging/staging*