

About Breast Cancer

Breast Cancer Basics

Get an overview of what breast cancer is, how it forms, and how common it is.

- What Is Breast Cancer?
- How Does Breast Cancer Start?
- How Common Is Breast Cancer?
- What's New in Breast Cancer Research?

Signs and Symptoms of Breast Cancer

The most common symptom of breast cancer is a new lump or mass, but other symptoms are also possible. It's important to have any breast change checked by a health care provider.

• Breast Cancer Signs and Symptoms

What Is Breast Cancer?

Breast cancer starts when cells in the breast begin to grow out of control. These cells usually form a tumor that can often be seen on an x-ray or felt as a lump. The tumor is malignant (cancer) if the cells can grow into (invade) surrounding tissues or spread (metastasize) to distant areas of the body. Breast cancer occurs almost entirely in women, but men can get breast cancer, too.

Cells in nearly any part of the body can become cancer and can spread to other areas. To learn more about cancer and how all cancers start and spread, see Cancer Basics.

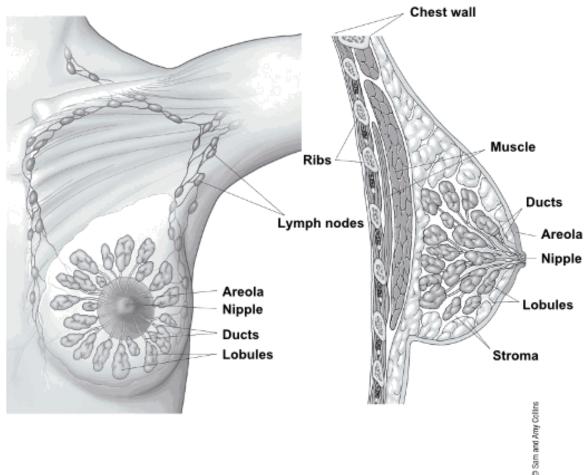
Where breast cancer starts

Breast cancers can start from different parts of the breast. Most breast cancers begin in the ducts that carry milk to the nipple (ductal cancers). Some start in the glands that make breast milk (lobular cancers). There are also other types of breast cancer that are less common.

A small number of cancers start in other tissues in the breast. These cancers are called <u>sarcomas</u> and <u>lymphomas</u> and are not really thought of as breast cancers.

Although many types of breast cancer can cause a lump in the breast, not all do. Many breast cancers are found on screening mammograms which can detect cancers at an earlier stage, often before they can be felt, and before symptoms develop. There are other symptoms of breast cancer you should watch for and report to a health care provider.

It's also important to understand that most breast lumps are benign and not cancer (malignant). Non-cancerous breast tumors are abnormal growths, but they do not spread outside of the breast and they are not life threatening. But some benign breast lumps can increase a woman's risk of getting breast cancer. Any breast lump or change needs to be checked by a health care professional to determine if it is benign or malignant (cancer) and if it might affect your future cancer risk.



Normal breast tissue

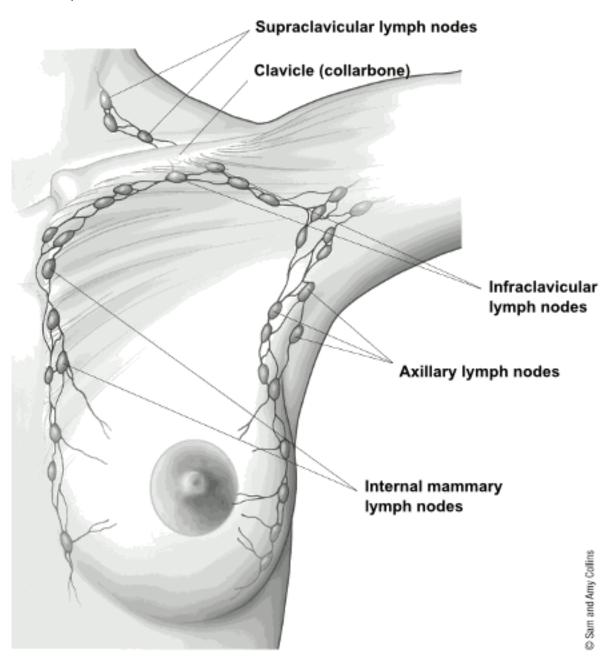
How breast cancer spreads

Breast cancer can spread when the cancer cells get into the blood or lymph system and are carried to other parts of the body.

The lymph system is a network of lymph (or lymphatic) vessels found throughout the body that connects lymph nodes (small bean-shaped collections of immune system cells). The clear fluid inside the lymph vessels, called lymph, contains tissue by-products and waste material, as well as immune system cells. The lymph vessels carry lymph fluid away from the breast. In the case of breast cancer, cancer cells can enter those lymph vessels and start to grow in lymph nodes. Most of the lymph vessels of the breast drain into:

Lymph nodes under the arm (axillary nodes)

- Lymph nodes around the collar bone (supraclavicular [above the collar bone] and infraclavicular [below the collar bone] lymph nodes)
- Lymph nodes inside the chest near the breast bone (internal mammary lymph nodes)



Lymph nodes in relation to the breast

If cancer cells have spread to your lymph nodes, there is a higher chance that the cells could have traveled through the lymph system and spread (metastasized) to other parts of your body. The more lymph nodes with breast cancer cells, the more likely it is that the cancer may be found in other organs. Because of this, finding cancer in one or more lymph nodes often affects your treatment plan. Usually, you will need surgery to remove one or more lymph nodes to know whether the cancer has spread.

Still, not all women with cancer cells in their lymph nodes develop metastases, and some women with no cancer cells in their lymph nodes develop metastases later.

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How Does Breast Cancer Start?

Changes or mutations in DNA can cause normal breast cells to become cancer. Certain DNA changes are passed on from parents (inherited) and can greatly increase your <u>risk</u> <u>for breast cancer</u>. Other lifestyle-related risk factors, such as what you eat and how much you exercise, can increase your chance of developing breast cancer, but it's not yet known exactly how some of these risk factors cause normal cells to become cancer. Hormones seem to play a role in many cases of breast cancer, but just how this happens is not fully understood.

Inherited versus acquired DNA mutations

Normal breast cells become cancer because of changes (mutations) in DNA. DNA is the chemical in our cells that makes up our genes. Genes have the instructions for how our cells function. Some DNA mutations are inherited or passed to you from your parents. This means the mutations are in your cells when you are born and some mutations can greatly increase the risk of certain cancers. They cause many of the cancers that run in some families and often cause cancer when people are younger.

But most DNA changes linked to breast cancer are acquired. This means the change takes place in breast cells during a person's life rather than having been inherited or born with them. Acquired DNA changes take place over time and are only in the breast cancer cells.

Mutated DNA can lead to mutated genes. Some genes control when our cells grow,

divide into new cells, and die. Changes in these genes can cause the cells to lose normal control and are linked to cancer.

Proto-oncogenes

Proto-oncogenes are genes that help cells grow normally. When a proto-oncogene mutates (changes) or there are too many copies of it, it becomes a "bad" gene that can stay turned on or activated when it's not supposed to be. When this happens, the cell grows out of control and makes more cells that grow out of control. This can lead to cancer. This bad gene is called an oncogene.

Think of a cell as a car. For the car to work properly, there need to be ways to control how fast it goes. A proto-oncogene normally functions in a way that's much like a gas pedal. It helps control how and when the cell grows and divides. An oncogene is like a gas pedal that's stuck down, which causes the cell to divide out of control.

Tumor suppression genes

Tumor suppressor genes are normal genes that slow down cell division (cell growth), repair DNA mistakes, or tell cells when to die (a process known as apoptosis or programmed cell death). When tumor suppressor genes don't work properly, cells can grow out of control, make more cells that grow out of control, and don't die when they should, which can lead to cancer.

A tumor suppressor gene is like the brake pedal on a car. It normally keeps the cell from dividing too quickly, just as a brake keeps a car from going too fast. When something goes wrong with the gene, such as a mutation, the "brakes" don't work and cell division can get out of control.

Inherited gene changes

Certain inherited DNA mutations (changes) can dramatically increase the risk for developing certain cancers and are linked to many of the cancers that run in some families. For instance, the BRCA genes (BRCA1 and BRCA2) are tumor suppressor genes. When one of these genes changes, it no longer suppresses abnormal cell growth, and cancer is more likely to develop. A change in one of these genes can be passed from a parent to a child.

Women have already begun to benefit from advances in understanding the genetic

basis of breast cancer. Genetic testing can identify some women who have inherited mutations in the BRCA1 or BRCA2 tumor suppressor genes (or less commonly in other genes such as PALB2, ATM or CHEK2). These women can then take steps to reduce their risk of breast cancer and make plans to look for changes in their breasts to help find cancer at an earlier, more treatable stage. Since these mutations in BRCA 1 and BRCA 2 genes are also associated with other cancers (besides breast), women with these mutations can also consider early screening and preventive actions for other cancers.

Mutations in tumor suppressor genes like the BRCA genes are considered "high penetrance" because they often lead to cancer. Although many women with high penetrance mutations develop cancer, most cases of cancer (including breast cancer) are not caused by this kind of mutation.

More often, low-penetrance mutations or gene variations are a factor in cancer development. Each of these may have a small effect on cancer occurring in any one person, but the overall effect on the population can be large because the mutations are common, and people often have more than one at the same time. The genes involved can affect things like hormone levels, metabolism, or other things that impact risk factors for breast cancer. These genes may cause much of the risk of breast cancer that runs in families.

Acquired gene changes

Most DNA mutations related to breast cancer take place in breast cells during a woman's life rather than having been inherited. These acquired mutations of oncogenes and/or tumor suppressor genes may result from other factors, like radiation or cancercausing chemicals. But so far, the causes of most acquired mutations that could lead to breast cancer are still unknown. Most breast cancers have several acquired gene mutations.

Tests to spot acquired gene changes may help doctors more accurately predict the outlook (prognosis) for some women with breast cancer. For example, tests can identify women whose breast cancer cells have too many copies of the HER2 oncogene. These cancers tend to grow and spread faster. There are <u>drugs that target</u> these cancer cell changes and improve outcomes for patients.

References

Bahcall O. Common variation and heritability estimates for breast, ovarian and prostate cancers. Nature Genetics. Accessed at www.nature.com/icogs/primer/common-variation-and-heritability-estimates-for-breast-ovarian-and-prostate-cancers/ on August

Shannon KM and Chittenden A. Chapter 80: Genetic Testing in Breast Cancer. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

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How Common Is Breast Cancer?

Breast cancer is the most common cancer in American women, except for skin cancers. Currently, the average risk of a woman in the United States developing breast cancer sometime in her life is about 12%. This means there is a 1 in 8 chance she will develop breast cancer. This also means there is a 7 in 8 chance she will never have the disease.

Current year estimates for breast cancer

The American Cancer Society's estimates for breast cancer in the United States for 2018 are:

- About 266,120 new cases of invasive breast cancer will be diagnosed in women.
- About 63,960 new cases of carcinoma in situ (CIS) will be diagnosed (CIS is non-invasive and is the earliest form of breast cancer).
- About 40.920 women will die from breast cancer.

Trends in breast cancer incidence

In recent years, incidence rates have been the stable in white women and increasing slightly (by 0.3% per year) African American women. Breast cancer is more common in these women, compared to women of other races/ethnicities.

Trends in breast cancer deaths

Breast cancer is the second leading cause of cancer death in women (only lung cancer kills more women each year). The chance that a woman will die from breast cancer is about 1 in 38 (about 2.6%).

Death rates from female breast cancer dropped 39% from 1989 to 2015. Since 2007, breast cancer death rates have been steady in women younger than 50, but have continued to decrease in older women.

These decreases are believed to be the result of finding breast cancer earlier through screening and increased awareness, as well as better treatments.

Breast cancer survivors

At this time there are more than 3.1 million breast cancer survivors in the United States. This includes women still being treated and those who have completed treatment.

Survival rates are discussed in the section on breast cancer survival rates by stage.

Visit the American Cancer Society's Cancer Statistics Center for more key statistics.

References

American Cancer Society. *Breast Cancer Facts and Figures 2017-2018*. Atlanta, Ga: American Cancer Society; 2017.

American Cancer Society. *Cancer Facts and Figures 2018.* Atlanta, Ga: American Cancer Society; 2018.

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

Lifetime Risk (Percent) of Dying from Cancer by Site and Race/Ethnicity: Females, Total US, 2010-2012 (Table 1.20)

http://seer.cancer.gov/csr/1975_2012/browse_csr.php?sectionSEL=1&pageSEL=sect_0 1_table.20.html.2014. Accessed August 9, 2017.

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Breast Cancer Signs and Symptoms

Knowing how your breasts normally look and feel is an important part of breast health. Finding breast cancer as early as possible gives you a better chance of successful treatment. But knowing what to look for does not take the place of having regular <a href="mailto:

The most common symptom of breast cancer is a new lump or mass. A painless, hard mass that has irregular edges is more likely to be cancer, but breast cancers can be tender, soft, or rounded. They can even be painful. For this reason, it is important to have any new breast mass, lump, or breast change checked by a health care professional experienced in diagnosing breast diseases.

Other possible symptoms of breast cancer include:

- Swelling of all or part of a breast (even if no distinct lump is felt)
- Skin irritation or dimpling (sometimes looking like an orange peel)
- Breast or nipple pain
- Nipple retraction (turning inward)
- Redness, scaliness, or thickening of the nipple or breast skin
- Nipple discharge (other than breast milk)

Sometimes a breast cancer can spread to lymph nodes under the arm or around the collar bone and cause a lump or swelling there, even before the original tumor in the breast is large enough to be felt. Swollen lymph nodes should also be checked by a health care provider.

Although any of these symptoms can be caused by things other than breast cancer, if you have them, they should be reported to a health care professional so that the cause can be found.

Because mammograms do not find every breast cancer, it is important for you to be aware of changes in your breasts and to know the signs and symptoms of breast cancer.

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What's New in Breast Cancer Research?

Researchers around the world are working to find better ways to <u>prevent</u>, <u>detect</u>, and <u>treat</u> breast cancer, and to improve the quality of life of patients and survivors.

Some of the many active areas of research include:

- Breast cancer causes
- Causes and treatment of metastatic breast cancer
- Reducing breast cancer risk
- Managing ductal carcinoma in situ (DCIS)
- New lab tests for breast cancer
- New imaging tests for breast cancer
- Breast cancer treatment
- Supportive care

Breast cancer causes

Studies continue to uncover lifestyle factors and habits, as well as inherited genes, that affect breast cancer risk. Here are a few examples:

- Several studies are looking at the effect of exercise, weight gain or loss, and diet on risk.
- Studies on the best use of genetic testing for breast cancer mutations continue at a rapid pace.
- Scientists are exploring how common gene variations (small changes in genes that are not as significant as mutations) may affect breast cancer risk. Gene variants typically have only a modest effect on risk, but when taken together they could possibly have a large impact.
- Possible environmental causes of breast cancer have also received more attention in recent years. While much of the science on this topic is still in its earliest stages, this is an area of active research.

Reducing breast cancer risk

Researchers continue to look for medicines that might help lower breast cancer risk, especially women who are at high risk.

- Hormone therapy drugs are typically used to help treat breast cancer, but some
 might also help prevent it. Tamoxifen and raloxifene have been used for many
 years to prevent breast cancer. More recent studies with another class of drugs
 called aromatase inhibitors (exemestane and anastrozole) have shown that these
 drugs are also very effective in preventing breast cancer
- Other clinical trials are looking at non-hormonal drugs for breast cancer reduction.
 Drugs of interest include drugs for osteoporosis and bone metastases, COX-2
 inhibitors, non-steroidal anti-inflammatory drugs, and statins (used to lower
 cholesterol).

When breast cancer spreads, it often goes to the bones. Some drugs that help treat the spread of cancer to the bones (such as bisphosphonates and denosumab), might also help reduce the chances of the cancer coming back. Studies done so far seem to suggest that postmenopausal women may benefit the most from giving these bonemodifying drugs after breast surgery, but more studies are needed to say for sure.

This type of research takes many years. It might be some time before meaningful results on any of these compounds are available.

Managing DCIS

In ductal carcinoma in situ (DCIS), the abnormal cells are in the milk duct and have not grown outside the duct. In some women, DCIS turns into invasive breast cancer, or sometimes an area of DCIS contains invasive cancer. In other women, though, the cells just stay within the ducts and never invade deeper or spread to lymph nodes or other organs. The uncertainty about how DCIS will behave can make it hard to choose the best treatments. Researchers are looking for ways to help with these challenges.

Researchers are studying ways to use computers and statistical methods to estimate the odds that a woman's DCIS will become invasive. Decision aids are another approach. They ask a woman with DCIS questions that help her decide which factors (such as survival, preventing recurrence, and side effects) she considers most important in choosing a treatment.

New lab tests

Tests for circulating tumor cells (CTCs)

Researchers have found that in many women with breast cancer, cells may break away from the tumor and enter the blood. These circulating tumor cells (CTCs) can be detected with sensitive lab tests. Although these tests can help predict which patients may have breast cancer that has spread beyond the breast (metastatic disease), it isn't clear if the use of these tests can tell whether the cancer will come back after treatment (recur) or help patients live longer. Some studies are looking at if these CTCs can be removed and then tested in the lab to determine which specific anticancer drugs will work on the tumor.

New imaging tests

Newer imaging methods are now being studied for evaluating breast changes that may be cancer.

Scintimammography (molecular breast imaging)

In this test, a slightly radioactive drug called a **tracer** is injected into a vein. The tracer attaches to breast cancer cells and is detected by a special camera.

This technique is still being studied to see if it will be useful in finding breast cancers. Some doctors believe it may be helpful in looking at suspicious areas found by regular mammograms, but its exact role is still unclear. Current research is aimed at improving the technology and evaluating its use in specific situations such as in the dense breasts of younger women.

Breast cancer treatment

Chemotherapy

It is known that <u>chemotherapy</u>can be helpful for many breast cancer patients. But predicting who will benefit the most or the least is still being studied. Sometimes there are significant side effects (long- and short-term) from chemotherapy, so having tests that can determine who really needs chemo would be useful. Many studies are being done to evaluate different tests that can more accurately tell which patients would benefit from chemo and which patients could avoid it.

Oncoplastic surgery

Breast-conserving surgery (lumpectomy or partial mastectomy) can often be used for

early-stage breast cancers. But for some women, it can result in breasts of different sizes and/or shapes. For larger tumors, it might not even be possible, and a mastectomy might be needed instead. Some doctors are addressing this problem by combining cancer surgery and plastic surgery techniques, known as **oncoplastic surgery**. This typically involves reshaping the breast at the time of the initial surgery, such as doing a partial breast reconstruction after breast-conserving surgery or a full reconstruction after mastectomy. Oncoplastic surgery may mean operating on the other breast as well to make the breasts more alike.

Triple-negative breast cancer

Since triple-negative breast cancers cannot be treated with hormone therapy or targeted therapy such as HER2 drugs, the treatment options are limited to chemotherapy. Other potential targets for new breast cancer drugs have been identified in recent years. Drugs based on these targets, such as kinase inhibitors and immunotherapy, are now being studied to treat triple-negative breast cancers, either by themselves, in combination, or with chemotherapy.

Targeted therapy drugs

<u>Targeted therapies</u> are a group of drugs that specifically target gene changes in cancer cells that help the cells grow or spread. New targeted therapies are being studied for use against breast cancer, including **PARP inhibitors.** These drugs are most likely to be helpful against cancers caused by *BRCA* gene mutations, and have shown some promise in treating some types of breast cancers. Olaparib (Lynparza) is now being used to treat women with *BRCA* mutations who have metastatic, HER2-negative breast cancer and who have already gotten chemotherapy. Other PARP inhibitors are also being studied.

Supportive care

There are trials looking at different medicines to try and improve memory and <u>brain symptoms after chemotherapy</u>. Other studies are evaluating if certain cardiac drugs, known as beta-blockers, can prevent the heart damage sometimes caused by the common breast cancer chemotherapy drugs, doxorubicin and epirubicin.

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look

at promising new treatments or procedures. Clinical trials are one way to get state-ofthe art cancer treatment. In some cases, they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials, or see <u>Clinical</u> <u>Trials</u> to learn more.

References

Adams S, Schmid P, Rugo HS. Phase 2 study of pembrolizumab (pembro) monotherapy for previously treated metastatic triple-negative breast cancer (mTNBC): KEYNOTE-086 cohort A. *Abstract 2017 ASCO annual meeting*.

Carmichael AR, Mokbel K. Evolving Trends in Breast Surgery: Oncoplastic to Onco-Aesthetic Surgery. *Arch Plast Surg.* 2016;43(2):222-223.

Cuzick, J et al. Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial. *The Lancet.* 2014;383 (9922):1041 - 1048.

de Pedro M, Baeza S, Escudero MT, et al. Effect of COX-2 inhibitors and other non-steroidal inflammatory drugs on breast cancer risk: a meta-analysis. *Breast Cancer Res Treat.* 2015;149(2):525-536.

Dizdar O, Arsian C, Altundag K. Advances in PARP inhibitors for the treatment of breast cancer. *Expert Opin Pharmacother*. 2015;16(18):2751-2758.

Gnant M, Van Poznak C, and Schnipper L. Therapeutic Bone-Modifying Agents in the Nonmetastatic Breast Cancer Setting: The Controversy and a Value Assessment. In Dizon DS, Pennel N, Rugo HS, Pickell LF, eds. *2017 American Society of Clinical Oncology Educational Book.* 53rd Annual Meeting. 2017.

Goss, P.E., et al., *Exemestane for Breast-Cancer Prevention in Postmenopausal Women.* New England Journal of Medicine, 2011. 364(25): p. 2381-2391.

Greene LR, Wilkinson D. The role of general nuclear medicine in breast cancer. *J Med Radiat Sci.* 2015;62(1):54-65.

Han HS, Diéras V, Robson ME et al. Efficacy and tolerability of veliparib (V; ABT-888) in combination with carboplatin (C) and paclitaxel (P) vs placebo (Plc)+C/P in patients (pts) with BRCA1 or BRCA2 mutations and metastatic breast cancer: A randomized,

phase 2 study. Abstract 2016 San Antonio Breast Cancer Symposium.

Henry NL, Bedard PL, and DeMichele A. Standard and Genomic Tools for Decision Support in Breast Cancer Treatment. In Dizon DS, Pennel N, Rugo HS, Pickell LF, eds. 2017 American Society of Clinical Oncology Educational Book. 53rd Annual Meeting. 2017.

Ignatiadis M, Lee M, and Jeffrey SS. Circulating Tumor Cells and Circulating Tumor DNA: Challenges and Opportunities on the Path to Clinical Utility. *Clin Cancer Res*; 21(21); 4786–800.

Mayer IA, Dent R, Tan T, et al. Novel Targeted Agents and Immunotherapy in Breast Cancer. In Dizon DS, Pennel N, Rugo HS, Pickell LF, eds. *2017 American Society of Clinical Oncology Educational Book*. 53rd Annual Meeting. 2017.

National Cancer INsitute. https://www.cancer.gov/about-cancer/treatment/clinical-trials/search. Accessed August 9, 2017.

Robson ME, Im SA, Senkus E et al. OlympiAD: Phase III trial of olaparib monotherapy versus chemotherapy for patients (pts) with HER2-negative metastatic breast cancer (mBC) and a germline BRCA mutation (gBRCAm). *Abstract 2017 American Society of Clinical Oncology Annual Meeting.*

Solin LJ, Gray R, Baehner FL, et al. A multigene expression assay to predict local recurrence risk for ductal carcinoma in situ of the breast. *J Natl Cancer Inst.* 2013;105:701-710.

Vliek SB, Meershoek-Klein Kranenbarg E, van Rossum AGJ et al. The efficacy and safety of the addition of ibandronate to adjuvant hormonal therapy in postmenopausal women with hormone-receptor positive early breast cancer. First results of the TEAM IIB trial (BOOG 2006-04). *Abstract 2016 San Antonio Breast Cancer Symposium.*

Yu M, Bardia A, Aceto N et al. Ex vivo culture of circulating breast tumor cells for individualized testing of drug susceptibility. *Science*. 2014 Jul 11; 345(6193): 216–220.

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