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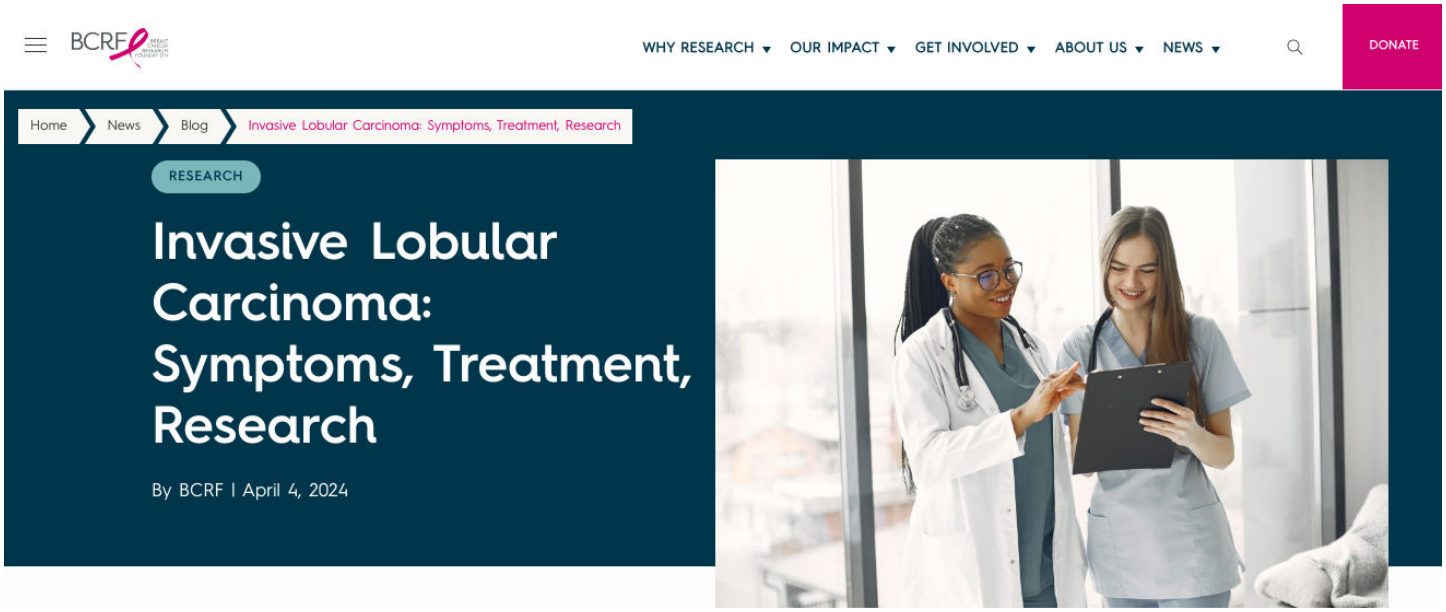

Learn more about lobular breast cancer and what BCRF is doing to accelerate lifesaving research

Invasive lobular carcinoma, also referred to as invasive lobular breast cancer (ILC) or simply lobular carcinoma/breast cancer, is the second most common type of breast cancer after invasive ductal carcinoma (IDC). The location where the cancer originates distinguishes ductal vs. lobular breast cancer: Invasive ductal carcinoma begins in milk ducts whereas invasive lobular carcinoma begins in lobules (the milk-producing glands of the breast).

Lobular breast cancer represents 10 to 15 percent of all invasive breast cancers. Over the past two decades, incidence rates of lobular carcinoma have increased. Approximately 43,700 cases of invasive lobular breast cancer were diagnosed in 2021, and this year as many as 47,000 could be diagnosed. Despite its prevalence, our understanding of the unique biology of lobular breast cancer is still emerging.

Lobular carcinoma is treatable but has a unique biology that affects symptoms, diagnosis, and therapeutic strategies. BCRF is working to better understand these challenges and advance lobular breast cancer research—and in just the last few years, say advocates and researchers like BCRF investigator Dr. Steffi Oesterreich, has made terrific progress. Our updated research regarding lobular carcinoma will help more patients around the world to find new treatments everyday.

What is invasive lobular carcinoma?

Invasive breast cancers are those that have broken out of the areas where they originated and infiltrated surrounding breast tissue. The most common type of invasive breast cancer is invasive ductal carcinoma, followed by invasive lobular carcinoma.

Ninety-five percent of invasive lobular carcinoma tumors are estrogen receptor (ER)–positive and 70 percent are progesterone receptor (PR)–positive. Sixty to 70 percent are both ER- and PR-positive. Lobular carcinoma typically expresses low or no HER2 protein (referred to as HER2-negative). These characteristics make lobular breast cancer a good candidate for endocrine therapies. However, invasive lobular carcinomas often become resistant to therapy.

Lifetime exposure to estrogen is a risk factor for breast cancers that rely on estrogen for growth. Factors that increase exposure to estrogen and progesterone, therefore, can increase risk of lobular breast cancer. These factors may include hormone replacement therapy and ages at menarche (first menstrual period), childbirth, and menopause—all of which contribute to lifetime hormone exposure. Alcohol consumption, which is a known risk factor for all breast cancers, appears to have a greater impact on risk of invasive lobular carcinoma vs. invasive ductal carcinoma.

The lobular form of breast cancer occurs more frequently in postmenopausal women and tends to be diagnosed at later, more advanced stages (more on that below). Lobular carcinoma is rare in men, representing less than two percent of all male breast cancers.

Lobular breast cancer has distinct biological characteristics that set it apart from ductal carcinoma. A hallmark feature of classical invasive lobular breast cancers is that the tumors grow in single-file strands rather than the more common "lump" seen in invasive ductal breast cancers. Other lobular breast cancers variants are characterized by distinct cell configurations, such as solid, honeycomb-like assemblies (alveolar), tube-like strands (tubule-lobular), and mixes of variants. These variants all have diffuse growth patterns that just slightly disturb the normal tissue architecture, making them harder to detect by physical exam or mammography.

The unique tumor growth patterns of lobular breast cancer are caused by a genetic alteration in the CDH1 gene that codes for E-cadherin, a protein that is essential for cell-to-cell adhesion that promotes normal tissue structure. A loss of CDH1 is the most prevalent gene alteration that distinguishes invasive lobular from invasive ductal cancer. Loss of E-cadherin function is associated with increased tumor development, invasiveness, and metastasis (spreading to distant sites in the body).

Lobular Carcinoma Diagnosis and Symptoms

How is lobular carcinoma diagnosed?

The diffuse growth pattern of lobular carcinoma can make diagnosis particularly challenging. In addition, these breast cancers are also more likely to be multi-focal (occurring in more than one location) or bi-lateral (occurring in both breasts), which complicates accurate screening, detection, and treatment.

Mammography and ultrasound—standard breast imaging tools—are less reliable for early detection of lobular breast cancer or recurrent disease. This can lead to later detection and a more advanced stage at diagnosis. Current research shows that MRI may be better able to detect lobular carcinoma than mammography, and new techniques are being developed, with several in clinical trials now.

Where does lobular breast cancer spread?

Lobular breast cancer can have a unique pattern of metastasis—spreading to distant sites of the body—compared to invasive ductal breast cancer. Both may metastasize to the bones, lungs, brain, and liver, though less frequently in lobular carcinoma. Unlike invasive ductal carcinoma, invasive lobular carcinoma tends to also spread to the ovaries, gastrointestinal tissues, and the peritoneum (the tissue surrounding the abdomen). Lobular breast cancer can recur and metastasize many years after diagnosis and treatment, so it is important to be aware of metastatic symptoms.

What are lobular breast cancer symptoms?

Like other breast cancers, lobular carcinomas may be detected before a person feels any symptoms through regular breast cancer screenings. Invasive lobular carcinoma symptoms tend to be similar to other breast cancers, but the structure of its formation is what sets it apart. Because it tends to form in a line instead of a lump, it can be harder to feel during a breast exam and harder to detect on a mammogram. Physical symptoms of lobular breast cancer are like those of other types of breast cancer and should be discussed with your health care provider.

The most common lobular breast cancer symptoms are:

- Hardened or thickened area inside the breast or underarm
- Dimpling, dent, or puckering of the skin of a breast
- Change in the size or shape of a breast
- Changes to the nipple, including inversion or pulling to one side
- A new area of fullness or swelling in the breast

Metastatic lobular breast cancer symptoms include:

- Unexplained and persistent bone pain, especially in the back, ribs, or thighs
- Unusual pelvic bleeding
- Abdominal pain, distention and/or bloating
- Difficulty eating or digesting food
- Unexplained weight loss
- Unexplained shortness of breath or painful breathing
- Frequent headaches, dizziness, or impaired cognitive function
- Swelling or lumps in the chest, armpit, neck, or groin
- Changes in skin color, lasting rash, or firm nodules on the skin
- New difficulty seeing

Lobular Carcinoma Treatment

Breast cancers are typically treated with a multidisciplinary approach involving surgery, radiation, and systemic therapies. Because of its diffuse and multi-focal nature, lobular carcinoma is difficult to detect both by imaging and during surgery. This characteristic also makes breast-conserving surgery more challenging. Unfortunately, up to 65 percent of people with lobular breast cancer require a second surgery.

The majority of these cancers are hormone receptor (HR)–positive, so endocrine (anti-hormone) therapies are typically administered for lobular breast cancer treatment. Most commonly, the anti-estrogen therapy tamoxifen is recommended for premenopausal women while an aromatase inhibitor such as letrozole or anastrozole is given to postmenopausal women. Although lobular breast cancer responds to hormone therapies, tumors can become resistant to treatment.

Invasive lobular carcinoma has generally been treated like HR-positive invasive ductal carcinoma, but there are marked differences in how the two types of invasive carcinoma respond to hormone therapies. This may be due to the unique biology of lobular breast cancer. Recent studies profiling lobular tumors suggest that some common genetic mutations cause a poorer response to hormone therapies and drive resistance. Researchers are working to target these genes to reverse the therapeutic resistance surrounding lobular invasive cancer. Lobular carcinoma generally does not respond well to chemotherapy because of its biological characteristics. A more profound understanding of the biology that distinguishes this disease subtype is critical for improving lobular breast cancer treatment.

The lack of clinical trials specific to lobular breast cancer continues to be a major barrier to advancing treatments for patients with this disease. Though invasive lobular carcinoma is not uncommon, it represents a smaller percentage of total invasive breast cancer cases and thus these patients are underrepresented in clinical trials. Researchers are striving to increase participation of patients with lobular breast cancer in clinical trials as well as designing clinical trials specifically focused on this subtype—achieving these goals is critical to advancing our understanding of lobular breast cancer and moving treatments and disease management forward.

BCRF's Lobular Breast Cancer Research

BCRF is the largest private funder of breast cancer research in the world and is working to support the rapidly growing and evolving field of lobular breast cancer research. In the past few years alone, there have been some exciting lobular breast cancer news—from deeper knowledge of tumor biology to leaps forward in technology to improvements in detection and diagnosis. More and more, breast cancer clinical trials are including women with lobular disease and a few trials are underway that are exclusively devoted to it.

We now know that lobular breast cancer tumors have enormous pathological and molecular diversity that affects how they form and respond to treatment. Progress in understanding the intricacies of the disease's biology has led researchers to develop new lobular carcinoma models for use in laboratory studies that subsequently inform new clinical trials. We have known that lobular breast cancer is understudied, which is why BCRF makes lobular breast cancer one of our priorities for future research initiatives.

Tremendous progress has been made in identifying the pathology of lobular breast cancer variants to diagnose individual patients' diseases more precisely. Researchers have identified molecular signatures unique to each variant and are now developing artificial intelligence-based strategies to find those features in images from tissue biopsies. Advancements are also being made in early detection by using molecular tracers that recognize and attach to lobular breast cancer cells, making them easier to find with screening technologies.

BCRF is at the forefront of lobular breast cancer research and continues to support work to:

- Understand the differences of lobular breast cancer variants
- Identify what causes metastasis to uncommon sites, such as the ovaries and peritoneum, compared to invasive ductal carcinoma
- Discover biomarkers to target the disease with immune therapy
- Investigate the drivers of lobular carcinoma development and growth
- Develop new ways to target and treat lobular breast cancer

International collaborations to make data accessible globally and increase awareness of the unique nature of invasive lobular carcinoma are shaping research and clinical management of this breast cancer subtype. In 2016, a community of researchers, doctors, patients, and advocates launched the International Invasive Lobular Carcinoma Symposium, in part, with BCRF support. Prior to this, there had not been a meeting with a specific focus on lobular breast cancer research. BCRF continues to sponsor this important conference, which was held virtually in 2021 and will convene for the third time in 2022.

In 2022, BCRF launched the Leigh Pate Living Biorepository of Invasive Lobular Breast Cancer, a first-of-its-kind repository overseen by BCRF investigators Drs. Steffi Oesterreich, Adrian Lee, and Jorge Reis-Filho. This biorepository was made possible through a legacy gift from lobular patient advocate Leigh Pate. Learn more about Leigh and this important initiative here. Additionally, you can listen to Dr. Steffi Oesterreich's interview with BCRF here.

BCRF is proud to support lobular breast cancer research and bring scientists and clinicians together to propel the field forward in hopes of finding new treatments for lobular invasive cancer. Looking to be updated with new information regarding lobular breast cancer? Add BCRF to your Google Discover, a mobile-only action, which will allow BCRF to send you updates to your mobile device with brand new information surrounding breast cancer news and lobular invasive carcinoma.

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