

FEATURE STORY

In Situ Breast Cancer: Is It Really Cancer?

BY BEVERLY A. CALEY

During a routine clinical exam, Judy Batchelor's doctor found a small lump in her left breast. By the time the lump was checked with a mammogram, it had disappeared. What the mammogram did show were deposits of calcium in the tissues of the right breast. Batchelor wasn't particularly concerned, since her mother's mammograms had identified calcifications for years and her mother was fine.

Although most calcifications don't indicate cancer, the doctor's office called three times to schedule a biopsy because of the suspicious pattern of Batchelor's calcium deposits, but Batchelor always told them she preferred watching the calcifications for any changes. Then one day the doctor called her personally, telling her that his sister died of breast cancer in her early 40s, and asked Batchelor to have the biopsy. It was 2004 and Batchelor was 40 at the time. "I gave in," she recalls. "He sounded genuinely concerned."

The surgeon who performed the biopsy told Batchelor she had stage 0 breast cancer, also known as ductal carcinoma in situ, or DCIS. What she thought would be no big deal turned into two surgeries and 33 radiation treatments.

The latin phrase "in situ," meaning "in place," is used in the context of cancer to describe abnormal cells that have not escaped the part of the body where they developed, thus DCIS specifically refers to abnormal cells in the lining of a milk duct that have not invaded surrounding breast tissue. Although these cells have the appearance of being precancerous when viewed under a microscope, they don't have the ability to spread as cancer cells would. Even so, a woman with DCIS has an increased risk of invasive breast cancer, ranging from two to more than eight times higher than the risk found in the general population.

[View Illustration: Progression of Noninvasive Breast Cancer](#)

Of the estimated 62,000 cases of in situ breast disease expected in 2006, about 85 percent will be DCIS. The remainder will have a less common disease known as lobular carcinoma in situ, or LCIS, which refers to abnormal cells contained within milk-producing lobules of the breast. Women with LCIS have a three to four

times higher risk of developing invasive cancer than the general population.

DCIS Questions and Controversies

Doctors are diagnosing seven times more cases of DCIS than in 1980. Many believe this rise occurred because of the increasing use of mammography to screen for breast cancer, and the growing frequency with which biopsies are performed on suspicious lesions. The questions surrounding this growing population of patients continuously leads to disagreement among doctors about whether these suspicious lesions should really be called cancer and what to do about them.

Melvin Silverstein, MD, director of the University of Southern California/Norris Lee Breast Center in Los Angeles, explains that an individual DCIS cell is genetically abnormal and in that sense, it is cancer. However, a property usually associated with cancer is that the abnormal cells have the ability to spread. According to Dr. Silverstein, since DCIS is biologically and genetically cancer but doesn't have the ability to spread, it could be considered a borderline cancer.

Michael Baum, MD, professor emeritus of surgery at University College London, says it may be more accurate to consider DCIS as a latent lesion that can go in a number of different directions. Dr. Baum explains that while some cases of DCIS progress to invasive cancer, many never cause any trouble and some spontaneously regress.

While doctors agree that not all DCIS cases progress to invasive cancer, it is difficult to determine which ones will progress since most DCIS lesions are surgically removed. Long-term follow-up studies of women with low-grade DCIS diagnosed before the era of widespread screening found that anywhere from 14 to 60 percent received a diagnosis of invasive cancer in the same breast where the DCIS occurred. Low- and intermediate-grade cells often look similar to normal cells and may indicate a lower risk of invasive cancer than high-grade cells. The National Comprehensive Cancer Network recommends that a second pathologist review a finding of DCIS to confirm that invasive disease is not present.

Despite the debate over whether or not it is cancer, DCIS is distressing to most women. Janice Stuff, a registered dietitian who is employed in the healthcare setting, says that even though she understood that having a diagnosis of DCIS was a very low-risk situation, she still panicked when she was diagnosed two years ago. As Batchelor notes, "Cancer can stir up fears, even when it has a 'stage 0' attached to it." However, some women, including 59-year-old Stuff, find a DCIS diagnosis is scarier than it needs to be. "I wish now, in retrospect, that I had been calmer about it. I've had dental procedures that have been more traumatic than the lumpectomy," Stuff recalls.



A persistent doctor led Judy Batchelor to find that she had a form of noninvasive breast cancer. Photo by Heather Rousseau.

Options for Treating DCIS

Most experts say that if DCIS is present in only one area and no abnormal cells are found at the edges of the first surgical excision, the primary treatment options are either a total mastectomy or a lumpectomy followed by radiation. Several studies have found that only 1 to 2 percent of women with DCIS later die of breast cancer, regardless of whether they had a mastectomy or breast-conserving surgery. However, mastectomy is usually recommended only if the margins of the tissue removed in a lumpectomy contain abnormal cells and the DCIS cannot be completely removed with repeat surgery.

Many patients treated with lumpectomy also undergo radiation therapy to kill any remaining abnormal cells in the breast tissue. The National Surgical Adjuvant Breast and Bowel Project B-17 trial tracked 818 women with localized DCIS to compare the results of lumpectomy alone versus lumpectomy plus radiation. It found that adding radiation reduced the occurrence of invasive breast cancer from 13.4 percent to 3.9 percent. However, since the overall mortality rate for patients in this study was only 1 percent, it is thought that the addition of radiation may have little effect on overall survival.

While radiation reduces the risk of invasive cancer, it does have side effects. Dr. Silverstein and his colleagues developed a system called the Van Nuys Prognostic Index, which for the past 10 years has helped doctors identify which women have a high risk of recurrence and would be most likely to benefit from radiation after lumpectomy or mastectomy. This system considers the size of the DCIS, the width of normal tissue at the edges of the removed tissue, how severely abnormal the cells appear and the patient's age at diagnosis. The higher the score, the greater the risk of recurrence and the more likely it is that the benefits of radiation will outweigh the side effects.

Beverley Anderson, RN, who works in the outpatient surgery department of a Houston hospital, has seen the terrible effects of cancer in friends, coworkers and patients. So in 2004 when faced with decisions about treatment for her DCIS, she chose an aggressive course of action. Her doctors explained the pros and cons of radiation treatment, and she chose to have radiation "just in case," she recalls.

Although doctors recommend surgery for DCIS, this position is not without controversy. Before the widespread use of screening mammography, most cases of DCIS were found because they caused symptoms, such as a palpable mass or serious nipple discharge. Now, most DCIS is discovered by routine mammography and has no symptoms, but not everyone thinks that discovering DCIS prior to the development of symptoms is entirely a good thing.

According to Dr. Baum, many women with DCIS have unnecessary mastectomies. He explains that in around 30 to 40 percent of cases, DCIS is multifocal—meaning it arises in more than one location. When multifocal DCIS is discovered, according to current thinking, a surgeon "has no choice but to carry out a mastectomy," Dr. Baum says. (The surgeon may suggest a sentinel node biopsy at the time of surgery to check for the possibility of invasive cancer.) Invasive breast cancers, on the other hand, are almost always unifocal—they arise in only one location. This leads to the paradox that the DCIS patient will lose her breast, when, if left alone, perhaps none of those lesions would have become invasive cancer. If one of them did become invasive cancer, it would almost certainly be unifocal and therefore treated with lumpectomy.

In contrast, Kent Osborne, MD, director of the Breast Center at Baylor College of Medicine in Houston, thinks that doctors must run the risk of overtreatment since there is currently no way of determining which lesions will lead to invasive cancer, although researchers are actively investigating the biological characteristics and evolution of precancerous breast lesions. In situ disease is so complicated that it takes years of experience and training to learn how to sort it all out, so experts advise women to find doctors they trust and take their advice.

Drug Therapy Options

Though the risk of recurrence eventually plateaus, there's about a 1 percent per year risk of DCIS returning in the same breast. Some doctors recommend that patients with DCIS, particularly those with a family history of breast cancer, take medication after treatment to prevent DCIS recurrence and the development of invasive cancer. Many take tamoxifen, which blocks the effects of estrogen in the breast. Recent data from a large study suggest that chemoprevention with tamoxifen should be reserved for postmenopausal women with DCIS that is estrogen receptor-positive since these types of cancer cells need estrogen to grow, and they may stop growing when treated with drugs that block the binding of estrogen.

The Study of Tamoxifen and Raloxifene (STAR) trial compared the effect of these two drugs in healthy women at high risk of developing invasive breast cancer. Data collected through the end of 2005 indicate that Evista (raloxifene) is as effective as tamoxifen in reducing the risk of invasive breast cancer. However, unlike tamoxifen, Evista does not reduce the risk of developing DCIS or LCIS. And these drugs are not without risks. Tamoxifen can cause cataracts, a side effect not associated with Evista, and while final data from the STAR trial indicate that the risk of other cancers, heart disease and stroke is about the same with both drugs, a separate study in women at high risk for heart problems found that while Evista reduced the risk of invasive breast cancer, it raised the risk of blood clots and fatal strokes. This latest study published in *The New England Journal of Medicine* in July 2006 included an editorial by Marcia Stefanick, PhD, of Stanford University School of Medicine, who said "the moderate benefits" of Evista for breast cancer prevention "do not seem to justify the risks."

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Other hormone therapies, such as Arimidex (anastrozole), Aromasin (exemestane), and Femara (letrozole), are thought to be effective in reducing the chance of cancer coming back, as either another DCIS or an invasive cancer. These aromatase inhibitors are being studied for postmenopausal women with DCIS that is estrogen receptor positive. Estrogen receptor-negative cells do not need estrogen to grow, and they usually do not stop growing when treated with drugs that block estrogen from binding. Dr. Osborne explains that research about treating this kind of cell is focusing on identifying the molecular pathways that

cause estrogen receptor-negative tumors to grow and finding ways to block those pathways.

Finding Answers

The best way to solve the disagreement about treatment of in situ breast cancer is to find a way to identify which lesions will lead to invasive cancer. Doctors anticipate this will be possible in the near future, possibly within five to 10 years, as a result of recent technologies that allow a genetic profile of all the different genes in a cancer cell to be generated. Researchers are hopeful that the particular set of genes that contribute to the formation of a tumor also dictate how aggressive that tumor will be. If so, it may be possible to identify the patterns that will allow doctors to predict which lesions will lead to invasive cancer.

Today, Anderson, Stiff and Batchelor are free of DCIS recurrence and invasive disease. While Batchelor recovered from her surgery, she read everything she could find about DCIS, but it left her with more questions than answers. “Would my DCIS ever have progressed into an invasive cancer? Was I overtreated? Did I need the radiation?” Batchelor says she wishes she had taken more time to learn about DCIS before she made her treatment decisions, but she doesn’t know that she would have done anything differently. “They don’t know whose DCIS will become invasive, so they can’t take a chance and do nothing. It’s sad and scary that we may be undergoing treatments that may not be necessary.”